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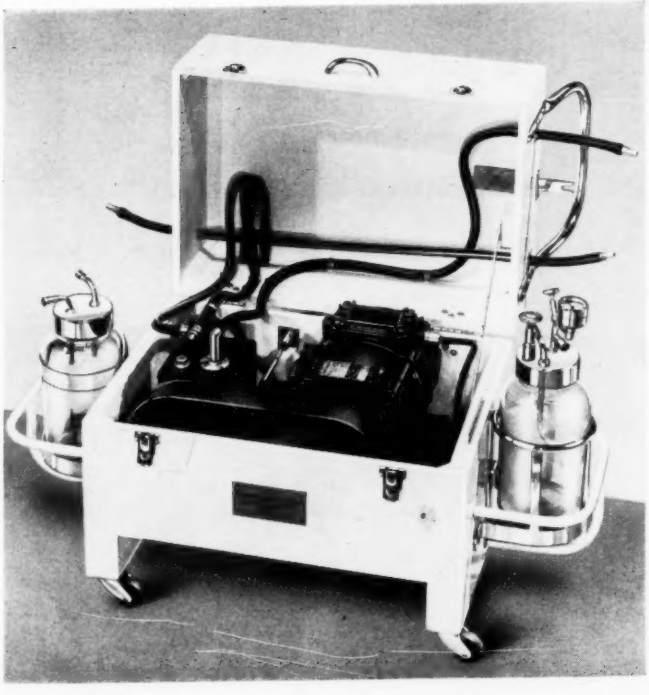

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BRITISH JOURNAL OF ANAESTHESIA

VOLUME XXIX No. 1 JANUARY 1957

EDITORIAL

FACULTY ELECTION

AN election to the Board of the Faculty of Anaesthetists of the Royal College of Surgeons is about to be held. There are on this occasion two vacancies and, judging from the experience of recent years, there will be a long list of aspirants. Few would suggest that membership of the governing board of an academic body such as the Faculty should be determined strictly on the grounds of geographical representation. Nevertheless recent elections would seem to indicate that residence outside the London Metropolitan area certainly does not increase a candidate's chances, although his academic claim may at least equal that of his London colleague. This is not necessarily in the interests of the faculty, which would probably be best served by a Board which, although primarily academically distinguished, is also reasonably representative.

ANAESTHETIC APPARATUS—FACTS WANTED!

MORE than one anaesthetist in the past found fame in a tap, a tube, a needle, or a bottle. These children of their inventive imagination were only too often born after a few casual chats to wise men of the calibre of King and Arcus, to mention but two in London, to whose workshop experience the final instrument owed much. If in the final event the instrument appeared to satisfy the simple practical needs of the anaesthetist everybody was satisfied.

Nowadays a new spirit is abroad. The anaesthetist not only wants and needs to know why an instrument works, but under what conditions it works best, and when it works well what its work consists of. The automatic respirator is a vastly more complex device than an endotracheal tube harness; a carbon dioxide absorber has more potential for harm than any specially shaped needle hub. There is a grave and widespread disquiet at the apparent inability or disinclination, or both, on the part of manufacturers of anaesthetic apparatus and instruments to supply essential information about their products, even when such information may be of vital importance to the patient's wellbeing. That this unhappy situation is not confined to anaesthesia is evident from a recent editorial in the *Lancet* (1956), which drew attention to the harm which had followed the use of the wrong kind of steel for bone fixation screws. Not only were the manufacturers castigated but so were the surgeons for apparently not being interested in such important details, although the facts were already known. The *Lancet* directed the attention of their readers to the need for defining responsibility for this " dangerous confusion ". A similar state of dangerous confusion may easily arise in the field of anaesthesia, if it does not already exist. Vaporizers for liquid anaesthetics are fitted to anaesthetic apparatus, but no information is supplied as to what concentrations might be expected to emerge from them in various circumstances. Carbon dioxide absorbers are offered without any scientific reasons based on experiment being given for their particular design. Soda lime of one sort or another is widely advertised—and indeed thrust on anaesthetists—with little if any experimental data about its chemical and physical behaviour in clinical circumstances. Expensive and complex automatic respirators, changing hands for several hundred pounds apiece, are being widely distributed through the country without any real information

of how they work or even that they do work in the way the anaesthetist expects or wants them to. Manufacturers apparently produce and sell these machines without any reference to physicists, physiologists, anaesthetists and others who could discover and give the required data. No information apparently exists, for none is supplied to the purchasers, as to what such equipment does to the patient. The first three papers in this issue are informative contributions, giving some indication of the "performance" of ordinary anaesthetic equipment likely to be in daily use.

Scientific fact about anaesthetic equipment is vitally important for the up-to-date anaesthetist who by his training is now able to digest them. It is high time that interest and reasonable demands in this direction were more insistent. The very least we can do for our patients is to beg for full information; the least we can do for our intelligence and conscience is to be loath to buy instruments in the future unless they are accompanied with sufficient explanatory and reliable data from the hands of competent investigators to make the use of such instruments intelligent and safe. The electronics industry, like most others, has for long recognized this need on the part of those using their products, and the very fullest data is always supplied with electronic equipment. The manufacturers of anaesthetic apparatus should do likewise. Anaesthetists must insist that they do.

REFERENCE

Editorial (1956). *Lancet*, **2**, 878.

ANOTHER STEP FORWARD

READERS will observe that we are printing this volume in a smaller type than hitherto. This has become necessary in order to cope with the flow of material. The Editorial Board is convinced that, although the number of articles in each issue will be increased, it will be possible to maintain the quality. Also for the same reason the Board has regretfully decided to omit, in future, routine reports of Society Meetings and their programmes, although it is hoped that papers of special interest read in the various thriving anaesthetic societies in the country will appear in these columns either in full or in abstract.

We would draw the attention of our contributors also to our intention in future to list in full the titles of articles to which reference is made. This should increase the value of any bibliography. There may be exceptions in this issue and the next, as certain papers were already in print when this decision was made.

Brit. J. Anaesth. (1957), **29**, 3

TRICHLOROETHYLENE CONCENTRATION FROM A " BOYLE " TYPE ANAESTHETIC APPARATUS

BY

W. W. MAPLESON

Department of Anaesthetics, Welsh National School of Medicine, Cardiff

INTRODUCTION

GILCHRIST and Goldsmith (1956) have recently criticized the trichloroethylene vaporizing unit of the Boyle type anaesthetic apparatus on the grounds that it can deliver " dangerously high " concentrations. They made a plea for the replacement of the present unit by a calibrated and standardized vaporizer.

In order to assess the value of such a proposal it seems essential to have a good knowledge of the performance of the present unit. Although Conn, Dyer and Ferguson (1955) have made some measurements of the concentrations obtained from a Marrett head on an Airmed apparatus, no detailed investigation of the Boyle apparatus appears to have yet been established.

METHOD

A British Oxygen Gases Ltd. Model H Boyle apparatus was used for the experiments. The trichloroethylene vaporizing unit of this apparatus is shown semidiagrammatically in figure 1.

Ports AA and BB are controlled by the rotation of a barrel tap: with the tap in the " off " position ports AA are closed and BB open so that the gas bypasses the vaporizing bottle. As the tap is opened ports AA gradually open and BB gradually close, thereby gradually increasing the proportion of gas passed through the bottle until, with the tap full on, ports AA are fully open and BB closed so that all the gas passes through the bottle.

A further control of concentration of trichloroethylene is provided by the plunger. By pushing this down the incoming gases are deflected to flow closer to the trichloroethylene surface and so produce more rapid vaporization.

The concentrations of trichloroethylene were determined by means of an infrared gas analyser through which a continuous sampling flow was drawn. In some experiments sampling was from the outlet of the vaporizing unit: this will be called " proximal sampling "—proximal as referred to the vaporizing unit. In other experiments the sample was drawn after the gas had passed through an anaesthetic system; usually the reservoir bag and corrugated tube of the Magill attachment

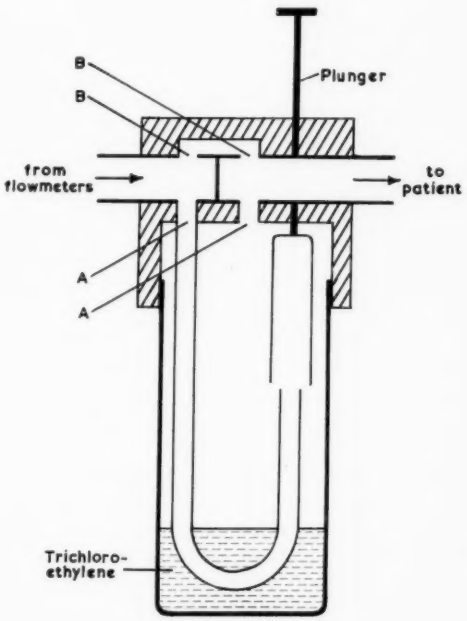


FIG. 1

Simplified cross section of the trichloroethylene vaporizer from a Boyle apparatus.

(System A, Mapleson, 1955). This will be referred to as "distal sampling".

In the distal sampling experiments the aim was to determine the concentration inhaled by the patient. As expected, this was generally less than that emerging from the vaporizing unit because the rubber of the anaesthetic system absorbs, or is porous to, the vapour. The inhaled concentration can be reliably determined without recourse to intermittent sampling provided that the concentration at the sampling point remains steady throughout inspiration and expiration. Clearly this will not be so if the sample is drawn near the expiratory valve with the system connected to a patient because of the vapour absorbed in the patient's lungs. The same was true in these experiments. An "artificial patient" was used consisting of a piston pump adjustable for rate and tidal volume and lubricated with an oil which absorbed trichloroethylene to a marked extent. The problem was solved by using the arrangement shown in figure 2 in which a tube of glass (which does not absorb trichloroethylene) whose volume was greater than the largest tidal volume used, separated the sampling point from the expiratory valve and pump. By displaying the quick response output of the analyser on an oscilloscope (Bracken, 1955) it was found that, after the first few breaths, the fluctuation within each respiratory cycle was only 5 per cent of the mean concentration and rapidly fell to only 2 per cent.* Thus the error in determining the inhaled concentration arising from the use of a continuous sample flow was generally only about 1 per cent of the measured concentration.

A further error can arise from absorption of vapour between the sampling point and the analyser. This was avoided by using polytetrafluoroethylene tubing to make this connection.

In each experiment the concentration was noted at intervals for a predetermined period after turning on the trichloroethylene tap. The zero and sensitivity of the analyser were checked at suitably short intervals. Total errors of measurement are generally less than 0.05 per cent trichloroethylene and rarely exceed 0.1 per cent trichloroethylene.

The results given below can be regarded as typical of this type of vaporizing unit but some variation must be expected between individual units. For instance: some recent experiments, in which four of these units were calibrated for use with Fluothane, showed that, although the general pattern of results was similar in all cases, the concentration obtained for any given condition varied by up to ± 20 per cent from the mean.

RESULTS

Some preliminary experiments showed that the factors which may affect the concentration of trichloroethylene inhaled by the patient are as follows:

(1) Distance from bottom of plunger to trichloroethylene surface.
(2) Tap setting.
(3) Gas flow.
(4) Degree of eccentricity of plunger and U-tube.
(5) Room temperature.
(6) Volume of trichloroethylene in bottle.
(7) Type of anaesthetic system connected to vaporizing unit.

*In this paper a variation or change in concentration is given as a percentage of the concentration existing under some specified condition and not as an actual percentage concentration. For actual concentrations the term "per cent trichloroethylene" is used, implying per cent trichloroethylene (v/v) in some gas. Although oxygen was used here the results would be the same for any mixture of perfect gases such as oxygen, nitrous oxide and air.

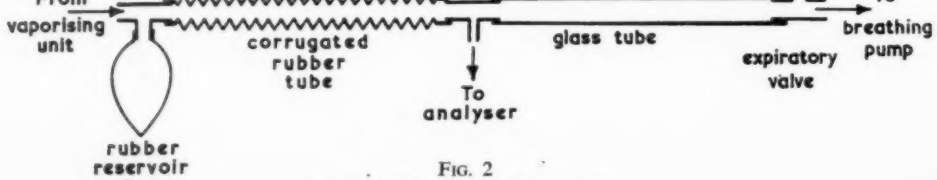


FIG. 2
Circuit used for distal sampling.

(8) Type of rubber used in anaesthetic system.
(9) Type of breathing.
(10) Time from turning on trichloroethylene.

In the laboratory factors 5, 6 and 10 can be replaced by a single factor: the temperature of the trichloroethylene. However, since a thermometer is not normally fitted in the vaporizing unit, it was felt the results could be more easily applied in clinical practice if presented in terms of the ten factors listed above.

If an average of only three different values were used for each of the first nine of these factors, then, to cover all combinations, a total of some $3^9 = 19{,}683$ experiments would be needed, each lasting an hour or more. However, the preliminary experiments indicated the general trend of the results and led to the selection of seventeen experiments, each lasting twenty minutes. The majority of these were designed to show, by proximal sampling, the influence of the first six factors on the concentration emerging from the vaporizing unit and the remainder, by distal sampling, how this concentration was modified, on its way to the patient, by factors 7 to 9. From the results of this main sequence, together with some information from the preliminary experiments, it is possible to estimate the inhaled concentration for most reasonable combinations of values with tolerable accuracy.

A few important results from the preliminary experiments will be considered first.

Preliminary Experiments

Variation of concentration with time. As would be expected from a consideration of the physical principles involved (Macintosh and Mushin, 1947) the trichloroethylene concentration, immediately after turning on the tap, was relatively high and fell with time—rapidly at first and then more and more slowly. In particular, with the plunger down, in the period from 20 to 60 minutes after turning on the tap, the concentration fell by only 10 per cent of the value at 20 minutes. With the plunger up the equivalent figure was 5 per cent. The fall was rather greater when gas was bubbled through the trichloroethylene, but this condition was not included in the main sequence of experiments. In one experiment observations were continued for two hours, with the plunger down, and in the second hour the concentration fell by 5 per cent of the value at 20 minutes.

Thus the experiments in the main sequence could be terminated after 20 minutes in the knowledge that the concentration-time curves could be extrapolated to two hours in accordance with the above figures.

Variation with degree of eccentricity of plunger and U-tube. In the vaporizing unit used for these experiments, as with many similar units, slackness in the sleeve bearing which guided the plunger allowed considerable play in the latter. Thus the plunger could be set so that it was not concentric with the U-tube. It was found that with a gas flow of 6 l./min and the plunger halfway down, moving the plunger from the concentric position to a position such that the inside of the plunger touched the outside of the U-tube at one point increased the trichloroethylene concentration by 20 per cent. In extreme conditions—at a flow of 2 l./min with the plunger up—such a manoeuvre can as much as double the concentration.

The undesirable nature of this feature is considered later. For the moment it is sufficient to say that in the main sequence of experiments this variable was eliminated by always setting the plunger concentric with the U-tube.

Variation with volume of trichloroethylene in bottle. Most of the preliminary experiments were conducted with 50 ml of trichloroethylene in the bottle at the start, but in a few 75 ml were used. The rate of fall of concentration was a little less in the latter cases because the trichloroethylene cooled more slowly but the effect was small. Therefore a volume of 50 ml was used throughout the main sequence of experiments. This gave a depth of liquid of a little over 2 cm and is of the same order as that commonly used in clinical practice.

"Standard" Conditions in the Main Sequence of Experiments

In describing the results of the main sequence of experiments it is convenient to state an artificial "standard" set of conditions involving one particular value for each of the factors listed at the beginning of the results section. Then each experiment shows the effect on the concentration

of varying one or more of these factors.

The standard set of conditions, then, was as follows:

(1) Distance from bottom of plunger to trichloroethylene surface at start of experiment: 70 mm.
(2) Tap setting: full on.
(3) Gas flow: 7 l./min.
(4) Plunger and U-tube: concentric.
(5) Room temperature: 24°C (75°F).
(6) Volume of trichloroethylene in bottle at start of experiment: 50 ml.
(7) Type of anaesthetic system: reservoir bag and corrugated tube (Magill attachment).
(8) Type of rubber: antistatic.
(9) Type of breathing: 330 ml tidal volume at 33 respirations per minute (to simulate the commonly occurring tachypnoea).

Items 7 to 9, of course, do not apply to the experiments with proximal sampling.

The effect of different values of each factor, except those already dealt with, will now be considered in detail, taking the experiments with proximal sampling first.

Proximal Sampling

Variation of concentration with distance from plunger to trichloroethylene surface. Besides the standard value of 70 mm (plunger fully up) values of 0 and 35 mm (plunger down and halfway respectively) were used. These were the distances at the beginnings of the experiments and consequently they gradually increased as the trichloroethylene evaporated. Figure 3 shows that the concentration is highest and falls most rapidly with the plunger down. The brief initial peak with the plunger up is attributed to saturated gas displaced from the bottle by the first few hundred ml of fresh gas after turning on the tap.

Gas was not bubbled through the trichloroethylene in the main sequence of experiments but the preliminary experiments showed that with otherwise standard conditions such a procedure would give from 5 to 3 per cent trichloroethylene for the first few minutes.

Variation with tap setting. In January, 1946, British Oxygen Gases Ltd. introduced a new design of tap. Although there was no change in the external features, the internal modification

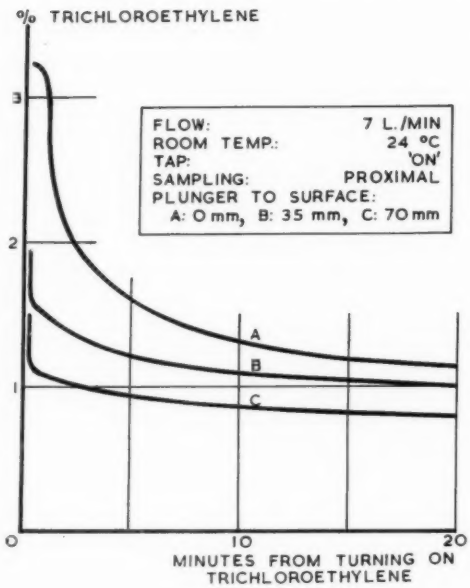


FIG. 3
Variation of concentration with distance from plunger to trichloroethylene surface.

considerably altered the way in which the concentration varied with tap setting. The unit used for the main sequence of experiments happened to contain an old style tap, so a few supplementary experiments were made with a unit incorporating a new style tap.

In both the old and new styles the " scale " beside the tap comprises four horizontal lines separating the words " off " and "on ". With both units experiments were made with the tap at each mark and at " on ", with otherwise standard conditions. For the unit with the old style tap it was found that with the tap at the 1st (adjacent to " off ") and 2nd marks no trichloroethylene vapour was obtained. With the tap at the fourth mark the concentration was the same as with it fully on. With the tap at the third mark the concentration at 20 minutes was about one-third of that with it fully on (see fig. 4). For the unit with the new style tap the results are shown in figure 5. It will be seen that here trichloroethylene vapour begins to appear when the tap is between

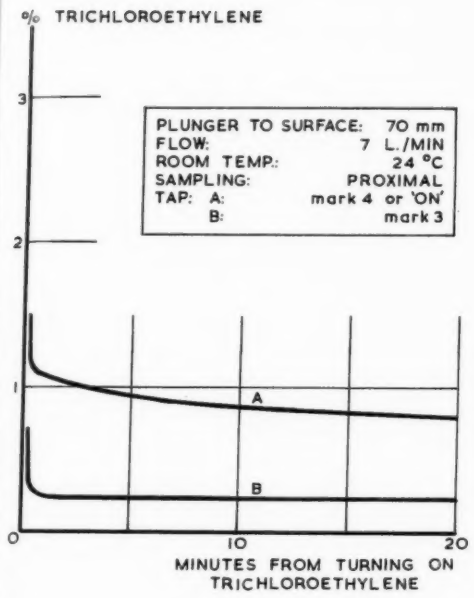


FIG. 4
Variation of concentration with tap setting—old style tap.

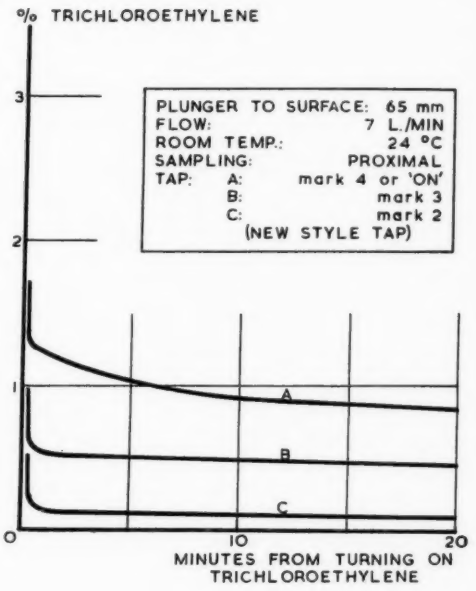


FIG. 5
Variation of concentration with tap setting—new style tap.

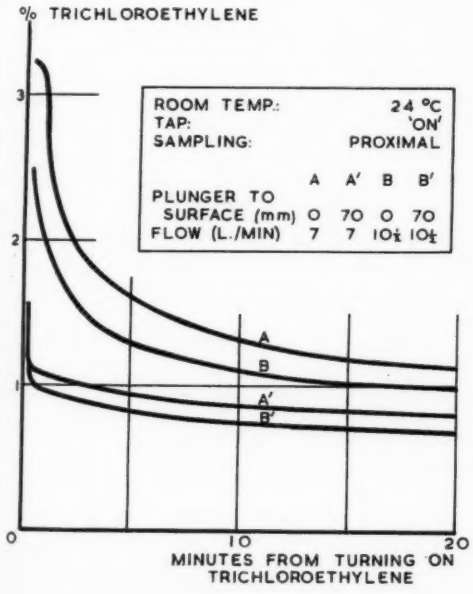


FIG. 6
Variation of concentration with gas flow—at two plunger-to-surface distances.

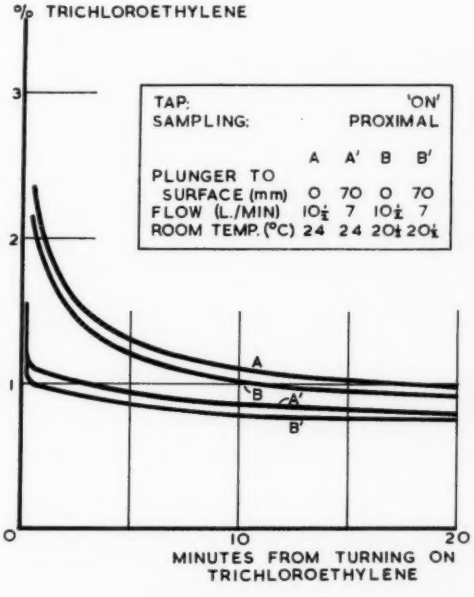


FIG. 7
Variation of concentration with room temperature—at two rates of vaporization.

the first and second marks and the concentration at 20 minutes then increases nearly linearly with tap setting up to the fourth mark.

Variation with gas flow. In two experiments an increased gas flow of 10.5 l./min was used. In one of these the conditions were otherwise standard, while in the other the plunger to surface distance was 0 mm. Figure 6 shows that increasing the flow has decreased the concentration by 15 to 20 per cent, of that at 7 l./min, with the plunger down and 10 to 15 per cent with the plunger up.

Variation with room temperature. For two experiments the room temperature was reduced to 20.5°C (69°F). In one of these the conditions were otherwise standard; in the other rapid vaporization was obtained by using a gas flow of 10.5 l./min with the plunger down. Figure 7 shows that in both cases reducing the room temperature reduced the initial concentration by 10 to 15 per cent and the concentration at 20 minutes by 5 to 10 per cent.

Distal Sampling

The effect of distal sampling. As mentioned earlier, rubber either absorbs or is porous to trichloroethylene vapour. It is to be expected, therefore, that the inhaled concentration will be less than that emerging from the vaporizing unit, particularly just after turning on the trichloroethylene. Figure 8 confirms this. Three pairs of curves show proximal and distal concentrations, all with standard distal conditions but with three different sets of proximal conditions covering a wide range of vaporization rates. It will be seen that the initial peaks in the proximal concentrations have been very much flattened in the corresponding distal concentrations. Also, the distal concentration gradually approaches the proximal concentration.

Variation with type of anaesthetic circuit and breathing. In addition to the reservoir bag and tube the T-piece and Cardiff perforated connector (Picken, 1950) systems were considered. In the first of these the gas is fed to the patient through a length of narrow bore tubing and a T-piece. Expiration and spillage of gas occurs through the free limb of the T-piece which may have a length of tubing attached to it. In the second system the T-piece is replaced by a short straight tube with a number of holes perforated in its wall. In both these systems, provided the gas flow is sufficient to eliminate rebreathing or the dilution of the anaesthetic with air, the breathing pattern cannot affect the inhaled concentration of vapour; since there is no reservoir bag the flow through the narrow bore tubing is constant and determined solely by the controls on the anaesthetic apparatus. Thus in these experiments the performance of both these systems could be examined merely by sampling from the end of a length of narrow bore rubber tubing without using the breathing pump. The particular tube used was 1.5 m long with a 6 mm bore. With the reservoir bag and corrugated tube, on the other hand, the breathing pattern will influence the flow in the rubber tubing and bag and hence affect the inhaled concentration. Accordingly, in addition to the "standard" respiratory pattern of 33 respirations per minute and 330 ml tidal volume, chosen to simulate the tachypnoea of established trichloroethylene anaesthesia, one experiment was done with 19 respirations per minute and 500 ml tidal volume—a pattern more characteristic of the induction stage.

Figure 9 compares the inhaled concentrations for these various distal conditions with the proximal concentration (curve A). The proximal conditions are the same in all cases. It will be seen that, unlike the reservoir bag and tube (curves C, D), the T-piece or perforated connector system (curve B) leads to only a slight flattening of the initial peak; the inhaled concentration is within 10 per cent of the proximal concentration after one minute. This is to be expected because of the smaller surface area of rubber and the thicker walls. (From this it can be deduced that the half-metre or so of narrow bore tubing sometimes inserted between the anaesthetic apparatus and the reservoir bag of the Magill attachment will have little effect on the inhaled concentration.) With the reservoir bag and tube the deeper slower respirations (curve D) lead to a more marked flattening of the peak than the "standard" respiratory pattern (curve C). This, also, is to be expected: in the extreme case of zero tidal volume the reservoir bag will remain distended so that it is effectively out of circuit, apart from diffu-

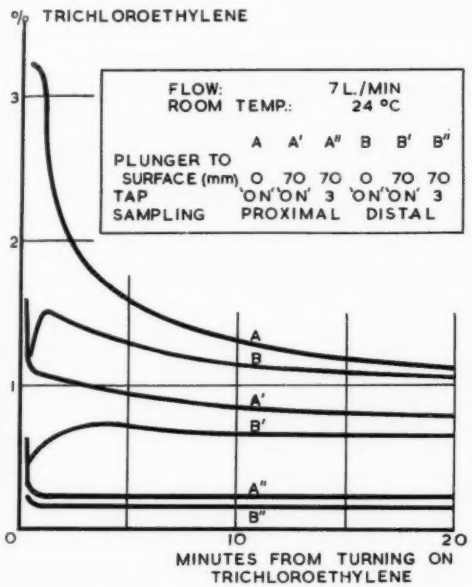


FIG. 8

Effect of distal sampling with reservoir bag and tube and 33 respirations per minute of 330 ml tidal volume —three rates of vaporization.

sion. As the tidal volume is increased the bag becomes effectively more in circuit, giving a greater area of rubber and greater absorption or diffusion of the vapour.

Variation with type of rubber. In all the experiments so far described antistatic rubber was used. One of these was repeated with a reservoir bag and tube in red rubber, but the results were identical with those obtained with antistatic rubber.

Note on the release of trichloroethylene from rubber. Since rubber absorbs trichloroethylene from the vapour stream it is to be expected that it will also release it back into the gas stream when the concentration is suddenly reduced. This was confirmed in one of the preliminary experiments by continuing distal sampling with the bag and tube after turning off the trichloroethylene. The concentration just before turning it off (60 minutes after turning it on) was 0.8 per cent trichloroethylene. This fell to 0.3 per cent trichloroethylene after one minute, to 0.1 per cent after four minutes and to 0.05 per cent after seven minutes.

Therefore, to be sure of consistent results in the distal sampling experiments, the bags and tubes were always allowed at least 24 hours "rest" from trichloroethylene before use.

DISCUSSION

The general pattern of the results is roughly what would be expected on theoretical grounds (Macintosh and Mushin, 1947), but a few points call for comment.

Firstly, in this vaporizing unit, short of bubbling gas through the liquid trichloroethylene, it is impossible to maintain concentrations much in excess of 1 per cent trichloroethylene. From informal inquiries among a small, but widely spread, group of anaesthetists it seems that this will generally be thought surprisingly low.

Another striking feature is the magnitude of the effect of vapour absorption in the reservoir bag and corrugated tube, particularly initially.

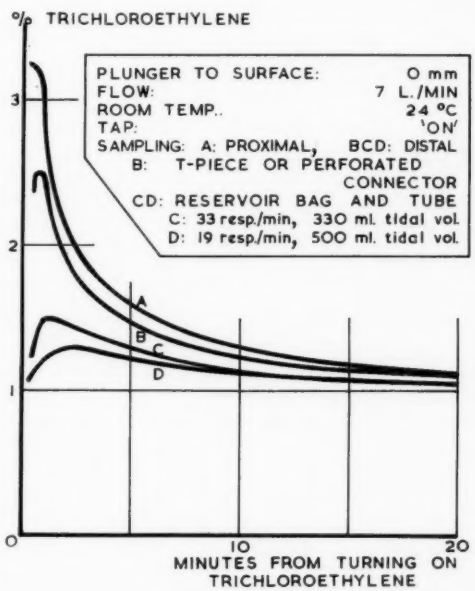


FIG. 9

Variation of inhaled concentration with anaesthetic system and breathing pattern.

However, when this is combined with the initially high concentration emerging from the vaporizing unit the resultant inhaled concentration is remarkably steady, particularly with the relatively slow and deep respirations of curve D in figure 9. In fact the variation is not a great deal more than would be expected from an elaborate vaporizer specially designed to eliminate such variations. Indeed, the performance of a vaporizer which, in itself, was theoretically perfect would be somewhat impaired by the absorption of vapour in the anaesthetic system.

The plunger and tap are intended to regulate the concentrations and do so quite effectively with the following reservations. Firstly, the old style tap has a very unsatisfactory relation between concentration and tap position, but this has been overcome in the new design. Secondly, any play in the plunger bearing gives rise to unwanted changes of concentration, but Hillard (1957) has devised a modification to overcome this. The other factors which influence the concentration (gas flow, room temperature and volume of liquid trichloroethylene) seem to have little effect within the ranges examined in these experiments.

Thus, given the improvement in the plunger guide and a more rigid quality control in manufacture, it would be practicable to compile a simple calibration table for the vaporizing unit when used with a reservoir bag and corrugated tube. With certain reservations such a table would generally be accurate to the nearest 0.25 per cent trichloroethylene.

The concentration obtained with combinations of conditions not specifically covered in these experiments can generally be estimated from a careful study of the graphs. If the conditions are changed some time after the trichloroethylene has been turned on the graph of concentration against time will jump to the curve representative of the new conditions but with some initial overshoot. For instance, if the plunger is pushed further down, the trichloroethylene temperature, and hence the emergent concentration, will be greater than if the plunger had been in the lower position from the start. However, the rate of cooling will also be greater, so that the discrepancy will gradually diminish. The reverse will occur if the plunger is raised. Absorption or release of vapour in the bag and tube will lead to these overshoots being partly smoothed out in the inhaled concentration.

Although Gilchrist and Goldsmith (1956) speak of "dangerously high" concentrations, they do not state what is the maximum concentration they would regard as safe. However, since the three figures they mention are 2.3, 1.6 and 0.9 per cent trichloroethylene, presumably 2.3 per cent would certainly be regarded by them as dangerous and perhaps also 1.6 per cent. Concentrations of these magnitudes can undoubtedly be obtained if gas is bubbled through the trichloroethylene. However, if this is avoided the maximum concentration which can be inhaled via a reservoir bag and corrugated tube is 1.5 per cent trichloroethylene and this rapidly falls to near 1 per cent.

CONCLUSION

Given the Hillard improvement of the plunger guide, the trichloroethylene vaporizing unit of the British Oxygen Gases Ltd Boyle type anaesthetic apparatus, when combined with the standard reservoir bag and corrugated tube, gives inhaled concentrations which vary remarkably little with time or, within reasonable limits, with other extraneous factors. Also, given the new style tap,* the control of this concentration is reasonably satisfactory. Provided gas is not bubbled through the trichloroethylene, the concentration inhaled through a reservoir bag and corrugated tube does not exceed 1.5 per cent trichloroethylene and cannot be maintained much above 1 per cent.

SUMMARY

The concentrations of trichloroethylene emerging from the vaporizing unit of a British Oxygen Gases Ltd. Boyle type anaesthetic apparatus and the concentrations inhaled by a patient through various anaesthetic systems have been measured in the laboratory under a wide variety of conditions. It has been found that although the curve of the concentration emerging from the vaporizing

*British Oxygen Gases Ltd. state that a new style tap can generally be fitted as a replacement part in old vaporizing units.

unit, against time, shows an initial peak, particularly with high rates of vaporization, the effect of the absorption of vapour by rubber is to reduce or even eliminate the peak when a reservoir bag and corrugated tube are used. If a T-piece or Cardiff perforated connector system with narrow bore tubing is used absorption of vapour is much less and the inhaled concentration differs little from that emerging from the vaporizing unit. If gas is not bubbled through the liquid trichloroethylene it is impossible to maintain concentrations much above 1 per cent trichloroethylene (v/v) when the bag and corrugated tube are used.

ACKNOWLEDGMENTS

The author's grateful thanks are due to Professor William W. Mushin for drawing attention to the problem and for his continuous encouragement; to E. K. Hillard, Esq., L.I.B.S.T., Senior Technician to this Department, for his great help in making many of the tedious observations involved; and to British Oxygen Gases Ltd. for their generosity in supplying two trichloroethylene vaporizing unit heads, and for the trouble they took to answer queries about the two styles of tap.

REFERENCES

Bracken, A., and Sanderson, D. M. (1955). Carbon Dioxide Concentrations found in Various Anaesthetic Circuits. *Brit. J. Anaesth.*, **27**, 428.

Conn, A. W., Dyer, A. E., and Ferguson, J. K. W. (1955) Factors Affecting Trichloroethylene Vapour Concentrations. *Canad. Anaes. Soc. J.*, **2**, 178.

Gilchrist, E., and Goldsmith, M. W. (1956). Some Observations on the Metabolism of Trichloroethylene. *Anaesthesia*, **11**, 28.

Hillard, E. K. (1957). A Modification to the Trichloroethylene Vaporizer on the "Boyle" Apparatus. *Brit. J. Anaesth.*, **29**, 39.

Macintosh, R. R., and Mushin, W. W. (1947). *Physics for the Anaesthetist*, p. 32, Oxford: Blackwell Scientific Publications.

Mapleson, W. W. (1954). The Elimination of Rebreathing in Various Semi-closed Anaesthetic Systems. *Brit. J. Anaesth.*, **26**, 323.

Picken, D. (1950). An Endotracheal connector for Infants. *Brit. med. J.*, **1**, 954.

BOOK REVIEW

The British Encyclopaedia of Medical Practice. Medical Progress and Cumulative Supplement (2nd edition), 1956. Published by Butterworth & Co., London. Pp. 364. Combined price 57*s*. 6*d*.

With the death of Lord Horder, the 1956 edition of *Medical Progress* appears with Lord Cohen of Birkenhead, as editor-in-chief. In the foreword, Lord Cohen pays tribute to his predecessor whom he regards as "one of the architects of contemporary clinical medicine . . . the first physician to bring the fruits of laboratory and instrument investigation to the bedside". As he points out, most of the arrangements for this volume were completed by Lord Horder, and the high standard set in previous issues is maintained.

On looking at the index under the heading Anaesthesia, one is referred to six abstracts which occupy about three pages of the 364-page book and these deal mainly with hypothermia. This must not be taken as indicative of the value of the book to the anaesthetist. In part II, which is devoted to Recent Advances in Pharmacology and Therapeutics, one finds an up-to-date discourse on chlorpromazine and such new drugs as methylpentynol, amiphenazole, and bemegride. With the increasing use of steroids the section on Cortisone and Related Steroids will prove extremely valuable to the clinician who has not the time to follow the numerous publications on these drugs. Likewise much valuable information can be obtained on the rauwolfia alkaloids.

New publications on hypothermia are appearing with amazing rapidity, especially in foreign journals; the time must have come for an authorative critical survey on this subject. It is hoped that such will appear in part I of the 1957 issue of *Medical Progress*.

In contrast to *Medical Progress*, the cumulative supplement "concerns knowledge of proved value and neither controversial nor doubtful material is included". In the absence of an index to the key numbers, it may be difficult to find Anaesthetic Trends in pages 38 and 39 (key number 34). The weakness of nitrous oxide-

[*Continued on page* 27

Brit. J. Anaesth. (1957), **29**, 12

PERCENTAGES OF FLUOTHANE VAPOUR DELIVERED FROM A TRILENE BOTTLE

BY

E. FALKNER HILL

IN an attempt to find an instrument that will give a known percentage of Fluothane vapour one is but following tradition. John Snow was the first anaesthetist to describe the effects produced by the inhalation of a known percentage of $CHCl_3$. He was followed by Clover with his chloroform inhaler, but he, convinced of the greater safety of ether, invented his well known ether inhaler. Paul Bert confirmed Snow's results and all were agreed that a high concentration of chloroform was the factor the most dangerous in the exhibition of chloroform. From this naturally follows the desirability of regulating the percentage of chloroform by the use of inhalers. So we come to Waller's well known chloroform balance and his less well known inhaler. Last of all the chloroform inhalers, the Vernon Harcourt. As chloroform became more and more replaced by ether, and later by trichlorethylene, attention was directed to inhalers giving known percentages of these and so we have the Macintosh Oxford vaporizer and a number of instruments for measuring the concentration of trichlorethylene.

Today, with the advent of Fluothane, it is equally desirable that the anaesthetist should know what percentage of Fluothane is producing the result he sees. He needs to know how to increase and decrease the percentage given and to be able to observe the conditions that result from such changes of strength.

When a gas—air, oxygen or nitrous oxide—passes through or over the surface of a volatile liquid such as chloroform or Fluothane it takes up a portion of that vapour. The amount taken up depends on the nature of the liquid, the surface exposed and the temperature.

The method I adopted to ascertain the percentage of Fluothane in a mixture with air or oxygen was very simple, namely to weigh a flask of known weight and capacity first with air or oxygen, and then with the mixture of air or oxygen with Fluothane that the apparatus I was testing gave.

This was an ordinary trichlorethylene bottle from a Boyle's apparatus fitted with an extended scale which ran from 0 to 10. Raventos (1956) had used such a bottle and had estimated the percentage of Fluothane coming over at 25°C and filled to different levels, namely 100 ml and 50 ml. These results do not imitate what occurs in the operating theatre. Figure 1 shows the direction in which the oxygen passes when the valve is (a) open and (b) closed. The scale is so arranged that at 0 all the oxygen passes by the bypass and at 10 all the oxygen passes over the Fluothane. As the lever is moved up the scale from 0 to 10 the opening to the chamber containing the Fluothane gets steadily larger, allowing an increasing portion of the gas flow to enter the chamber and pick up more and more Fluothane. Oxygen at the rate of 10 litres a minute was passed through the trichlorethylene bottle and into the flask of 600 ml capacity and samples taken at scale points 4, 5, 6, 7, 8, 9, 10, and the flask and its contents weighed after each point. The results are shown in graph I.

Graph II shows what happens when the rate of flow is maintained at 10 litres, the proportion of oxygen going over the Fluothane being kept steady by retaining the tap in the same position throughout. Curves for points (taps) 9, 8, 7, 6, are shown.

Graph III shows at a glance the percentage that is being used.

As this method is obviously very extravagant and as Fluothane has no effect on soda lime, a series of experiments were made with the oxygen

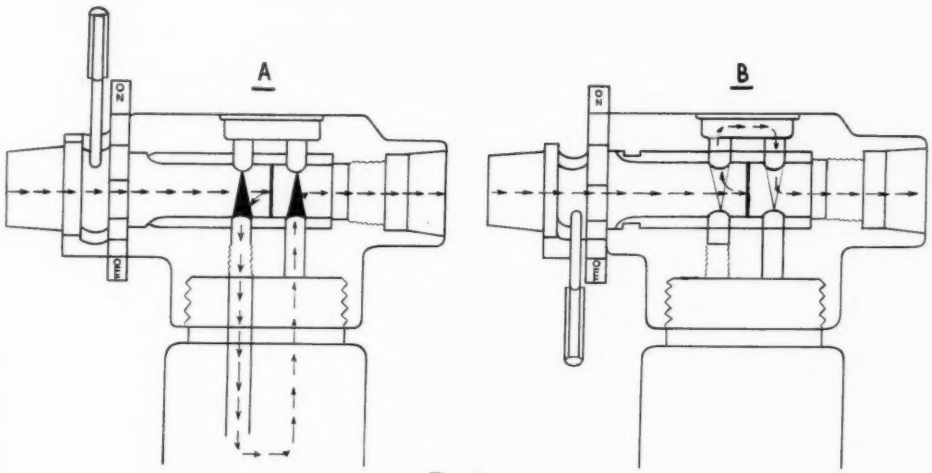
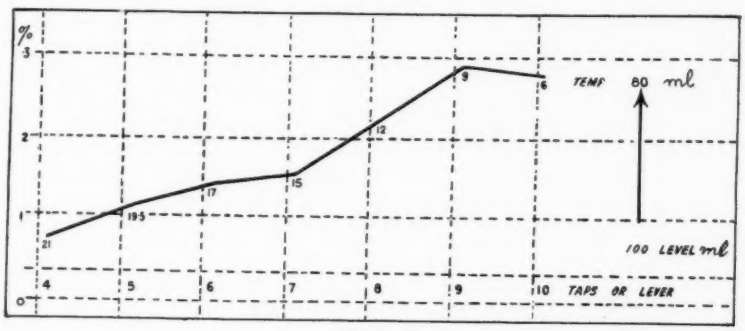


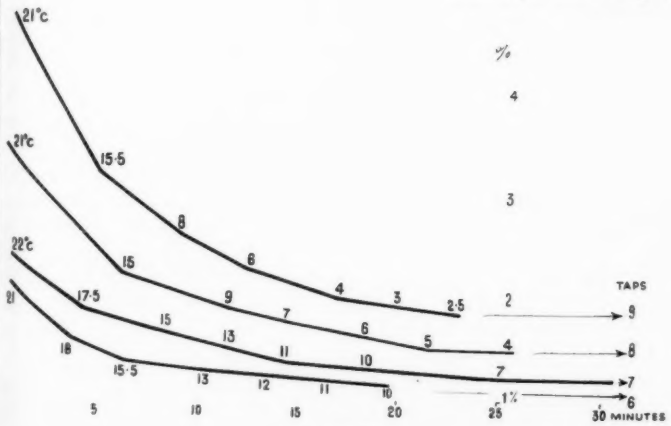
FIG. 1

Travel of gases into and out of the bottle: (A) with valve open; (B) with valve closed.



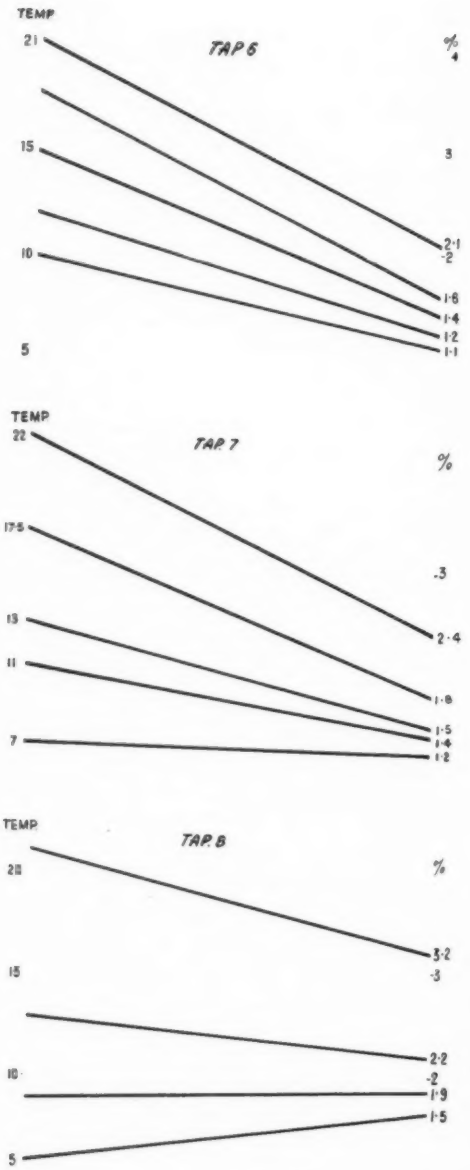
GRAPH I

10 litres per min. Plunger pulled out.



GRAPH II

Shows the steady fall of temperature which occurs with a steady flow of 10 litres and same tap. 10 litres per min. Plunger at top.



GRAPH III

Shows percentage being used at varying temperatures with taps 6, 7 and 8. 10 litres per min. Plunger at top.

running at 3 litres a minute. These experiments were made with another bottle supplied by the B.O.C. in which the U-shaped tube with plunger was replaced by a single tube closed at the end, but perforated about 1 cm above the 100 ml mark by an opening, the diameter of which is about that of the tube. Similar graphs to those made with the other bottle with the gas running at 10 litres a minute were made and are here produced (graphs IV, V, VI). If it is found practical to use this flow in a closed circuit it is obviously desirable to do so.

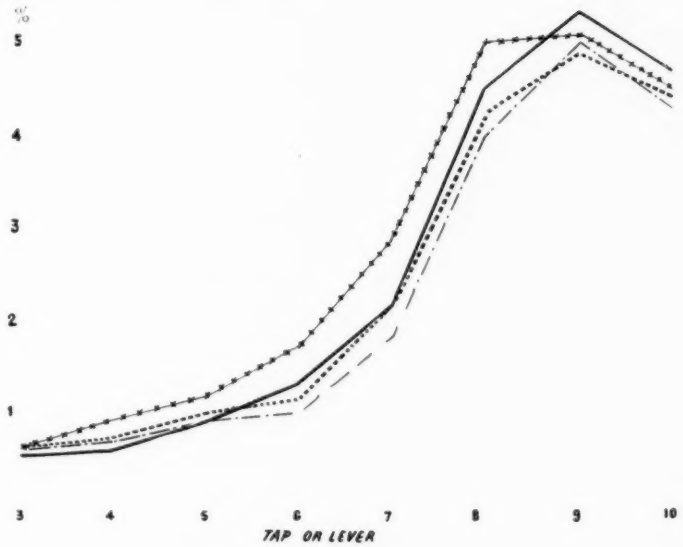
Study of the graphs shows that the percentage at any given moment is the resultant of a number of factors, the chief of which are the rate of flow of the oxygen and the fall of temperature caused by the evaporation of the Fluothane. There are other factors of lesser importance, such as the level of the liquid below the opening. In these experiments some error will have crept in here because the divisions on the Fluothane bottle were at 10 ml intervals so that any intermediate level was a matter of estimation.

The calculation is made as follows:

1 litre of Fluothane vapour weighs	8.9 g.
1 litre of oxygen weighs	1.42 g.
Difference	7.48 g.
Capacity of weighing flask	600 ml.

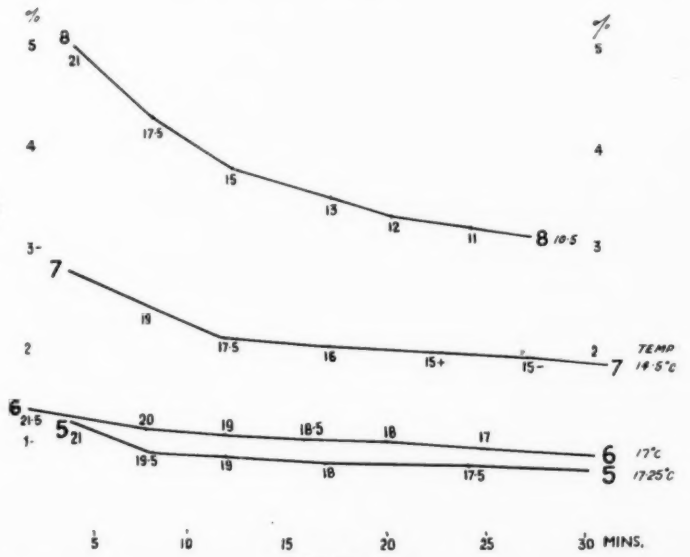
600 ml of Fluothane vapour weighs 600×7.5 mg = 4500 mg more than 600 ml of oxygen. Such a flask contains 100 per cent Fluothane. If the increase in weight after any experiment be divided by 45 we shall get the percentage of Fluothane that it contains: each 45 mg = 1 per cent.

If we examine the four curves in graph IV we shall see that the four curves which ought to be identical are not and that at tap 7 the highest curve shows a percentage 1.1 higher than the lowest. If now we look at graph V we see that the percentage of Fluothane coming over does in fact vary by about so much as 1 per cent and this variation is in the main due to the change in temperature. It is also obvious that a curve made from observations at minute intervals would be more nearly vertical and to the left of the four illustrated while a curve made at 15 minute intervals would be more nearly horizontal and would occur to the right of those depicted.



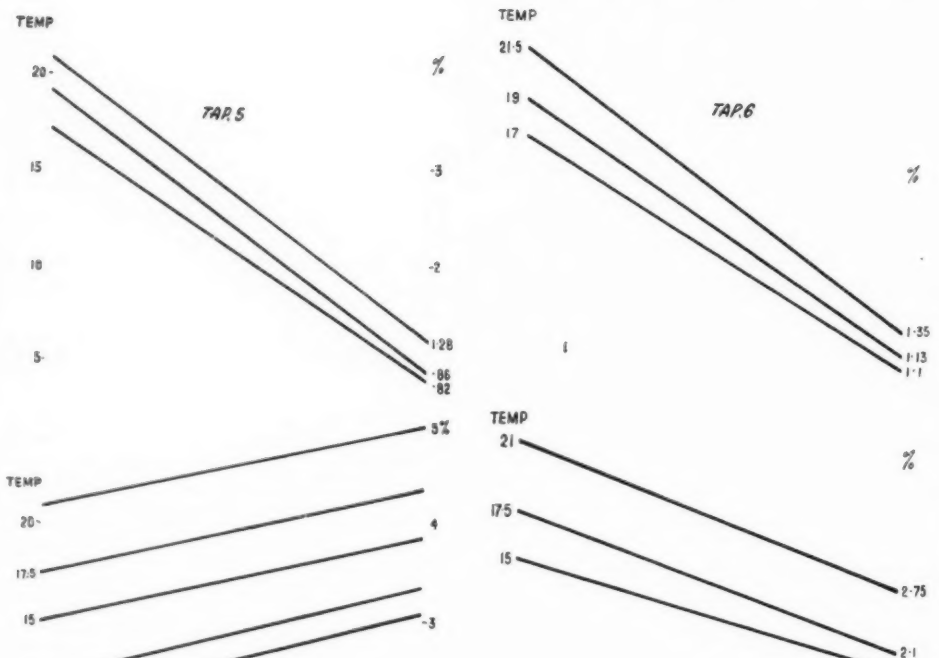
GRAPH IV

3 litres per min.
Single stem bottle with side opening.
These curves took between 29 and 32 minutes, and would account for some of the differences in them. The observations were made at 3, 4, and 5 minute intervals.



GRAPH V

3 litres per min.



GRAPH VI
3 litres per min.

Graph VI does in fact take account of some of these sources of error and should prove a practical guide to the anaesthetist in his early trials with Fluothane.

The figures given are those that were found under the conditions existing at the time of the experiments; they have not been reduced to 0°C and 760 mm pressure. In the 10-litre series the plunger was always at the top.

REFERENCES

Raventos, J. (1956). *20th Int. Phys. Cong. Abs. Brussels*, p. 754.

Brit. J. Anaesth. (1957), **29**, 17

MODEL EXPERIMENTS ON ABSORPTION EFFICIENCY OF SODA LIME

BY

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IN the field of general anaesthesia the maintenance of a normal carbon dioxide tension in the patient's arterial blood is still a central problem dependent on a number of factors. The experiments discussed here apply to only one of these factors, namely, the efficiency of carbon dioxide absorption by soda lime in a closed system.

What the requirements for soda lime's efficiency are, or expressed in another way, how high the concentration of carbon dioxide in inspired air can be before it must be regarded as harmful to the patient, cannot be answered in general terms. Though carbon dioxide in inspired air must be regarded as undesirable, experience indicates that carbon dioxide absorption can be regarded as satisfactory as long as the amount of carbon dioxide present in inspired air does not exceed 0.6 per cent, as has been suggested by Mousel et al. (1946).

The results of a number of experiments on the ability of soda lime to absorb carbon dioxide under varying conditions will be reported here.

In a previously published study by Lund et al. (1956) adult volunteers were breathing through an ordinary Waters canister filled with soda lime. The amount of carbon dioxide which passed through the canister without being absorbed was determined. The amount of carbon dioxide which at any time was absorbed by the soda lime was expressed as a percentage of the amount of carbon dioxide produced by the individual. This was used as an expression of the absorption efficiency of the soda lime. When this efficiency is 90 per cent it means that 90 per cent of the carbon dioxide in the expired air will be absorbed by the soda lime, while 10 per cent goes through. If, therefore, the expired air of the subject contains 3 per cent carbon dioxide, this air will come out of the canister containing 0.3 per cent.

During these experiments the carbon dioxide content of expired air was about 3 per cent, and if one applies the previously mentioned limit for the applicability of soda lime of 0.6 per cent carbon dioxide in the inspired air this corresponds to an absorption efficiency of 80 per cent.

Figure 1 shows the result of an experiment with two different types of soda lime, A and B. The absorption efficiency of type A was approximately 80 per cent after one hour, while that of type B decreased to about 60 per cent in the same length of time, meaning that the expired air still contained 1.2 per cent carbon dioxide after passing through the canister.

Owing to the large variation in efficiency found in these experiments it was thought to be desirable to supplement these investigations with model experiments aimed at elucidating the influence of the flow rate and the degree of humidity of the respiratory gases on the efficiency of the soda lime.

METHOD

An ordinary Waters canister was filled with about 425 grams soda lime. From a cylinder a gas mixture containing 4–7 per cent carbon dioxide was passed through the canister at rates of 15–39 litres per minute. In some experiments dry gas at room temperature was used and in others gas at 37°C, saturated with water vapour.

The gas leaving the canister was led into a spirometer in which the carbon dioxide was completely absorbed by 10 per cent potassium hydroxide running over saddle-formed pieces of porcelain. The resulting decrease in volume was registered, thus giving a continuous record of the quantity of carbon dioxide absorbed per minute (Erikson et al., 1951).

The water vapour tension and temperature in

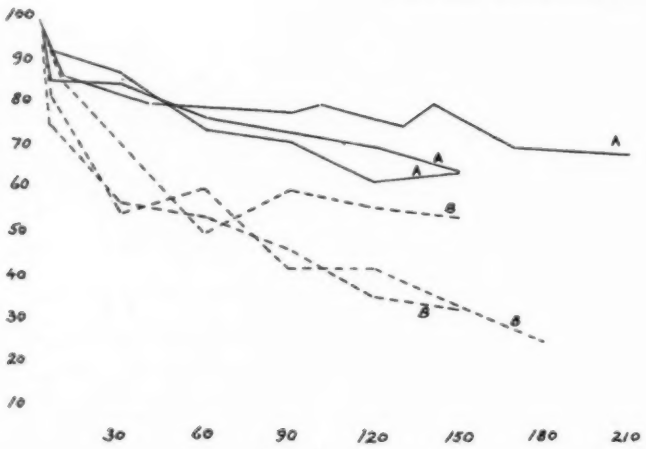

FIG. 1

CO_2 absorption efficiency of two different types of soda lime tested on human subjects.

Ordinate: Abs. Eff. % Abscissa: Time in minutes.

this system was kept constant. The carbon dioxide quantity could, in this way, be determined with an accuracy of ± 5 ml of carbon dioxide.

Three different brands of soda lime were investigated, to be called A, B and C. A was the most coarse grained, B was finer grained and C was so fine that resistance had to be regarded as a handicap.

RESULTS

Figure 2 shows carbon dioxide absorption efficiency under the conditions mentioned.

In the upper curves a gas mixture containing from 5.2 to 7.3 per cent carbon dioxide was being used with a flow through the canister of about 16 l./min (14.6–17.8 l./min). This flow probably corresponds to the maximum flow rate during resting ventilation with a minute volume of 6–7 litres.

If we regard as acceptable a carbon dioxide percentage up to 0.6 in the gas leaving the canister, and if instead of litres carbon dioxide absorbed as stated in figure 2 we assume a carbon dioxide production of 200 ml/minute, the findings indicate that for the soda lime types A and B efficient carbon dioxide absorption lasts for a little more than two hours, whereas type C is effective for a little less than four hours

If the same gas mixture is warmed up to 37°C and saturated with water vapour the soda lime absorbs carbon dioxide with the same degree of

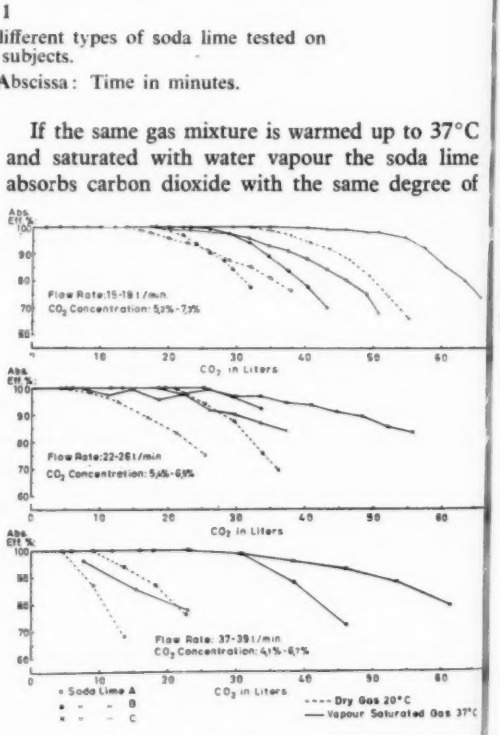

FIG. 2

CO_2 absorption efficiency of three different brands of soda lime in model experiments with dry gas at room temperature and gas at 37°C. saturated with water vapour with varying flow rates.

efficiency for 3 hours 15 minutes, 2 hours 45 minutes, and 5 hours respectively.

When the flow is increased to approximately 24 l./min (22–26.1 l./min), corresponding to the maximum flow rate during a ventilation of about 10 l./min, we find absorption efficiency reduced.

If the gas mixture is dry the A and B types of soda lime absorb efficiently for 1 hour 45 minutes and 2 hours 20 minutes respectively, while if the gases are saturated with water vapour types A and B give efficient absorption for about 2 hours 30 minutes and type C for about 4 hours.

When the flow is further increased to approximately 38 l./min (37.2–38.5 l./min), corresponding to the maximum speed of flow during a ventilation of 15 l./min, there is another great reduction in absorption efficiency. With dry gas the canisters filled with soda lime types A and B now function efficiently for 45 minutes and 1 hour 30 minutes only. With humid gas the efficiency of types A, B, and C lasts for approximately 1 hour, 2 hours 15 minutes, and 4 hours respectively.

It has been asserted that turning the canister 180°, or, rather, reversing the gas flow, should increase carbon dioxide absorption efficiency in a soda lime canister, because the gas should in this way come into contact with new unused portions of the soda lime. Figure 3 shows the results as regards carbon dioxide absorption efficiency when this is done. It is evident from the figure that when fresh soda lime was being used no increase in the efficiency was achieved. On the other hand, soda lime which had been kept in an open container for some time showed a slightly increased efficiency when the gas flow was reversed.

Without attempting to explain this difference we merely wish to point out that turning the canister is not a reliable method of increasing carbon dioxide absorption.

To get an idea of how important the size of to soda lime grains is to the resistance, the latter was determined at a flow of 22 l./min. A resistance of 1 mm, 2 mm and 6 mm of water was then found for the canisters filled with soda lime of types A, B and C respectively.

Our experiments are in good agreement with findings of previous investigators, namely, that absorption efficiency of soda lime is at a maximum when the gas is moist and that high rates of flow reduce efficiency. The effect of the humidity on the soda lime's absorption efficiency was comparatively small at a low flow rate and greater at increased flow.

When we compare the three different types of soda lime used in these experiments it is seen that their absorption efficiency also varied to a

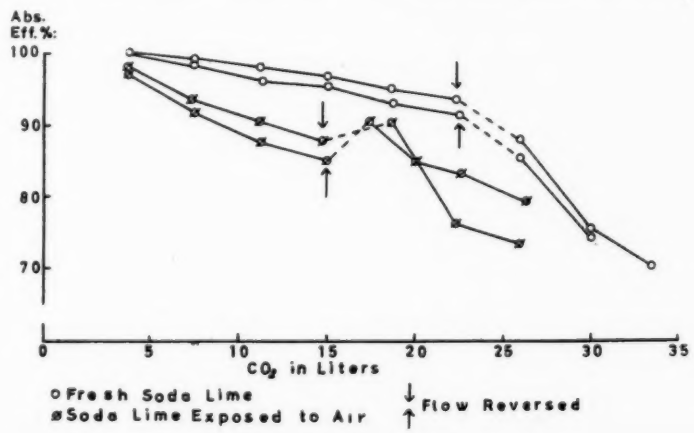

FIG. 3

CO_2 absorption efficiency of fresh soda lime and the same brand of soda lime exposed to air when the gas flow is reversed.

certain extent at low flow speed, while at increased speed the difference became greater. The most coarse-grained soda lime, A, displayed the least absorption efficiency. The fine-grained C was the best, but this type must be regarded as less suitable because of too great resistance.

We have used flows ranging from 15 to 40 l./min in our experiments. It is a most likely estimate that flow rates of this magnitude may be encountered during ventilations in the range of 6 to 16 l./min, provided the type of ventilation is even and regular.

CONCLUSION

If we assume a carbon dioxide production of about 200 ml/min, and if we accept a carbon dioxide of 0.6 per cent in the inspired air, soda lime types A and B give sufficiently good absorption for about 3 hours, provided that ventilation is even and does not exceed about 7 l./min.

If ventilation increases to about 10 l./min the same types of soda lime are equally efficient for 2 hours 30 minutes and 3 hours respectively, while at ventilations of about 15 l./min satisfactory absorption will last for 1 and 2 hours only.

The fact that absorption efficiency is, as our experiments show, to such a great extent dependent on the rate of flow through the canister explains why the efficiency varies with the type of respiration. A brief increase in ventilation because of any irregularity of respiration, such as coughing, for instance, will immediately reduce absorption efficiency. The carbon dioxide content in inspired air will increase. This in turn increases ventilation, and thus the speed of flow through the canister. In this way a vicious circle is established leading to an inefficient carbon dioxide absorption in many instances.

One should bear this in mind also when controlled ventilation is being used. A too energetic artificial ventilation will thus automatically result in a poorer absorption.

If the expired air cools and loses humidity before it reaches the canister the soda lime's efficiency is also reduced.

REFERENCES

Erikson, H., Scholander, P. F., and Irving, L. (1951). Apparatus for Complete Volumetric Recording of the Respiratory Gaseous Exchange. *Scand. J. Clin. Lab. Invest.*, **3**, 228.

Lund, I., Lange Andersen, K., and Erikson, H. (1956). Efficiency of Carbon Dioxide Absorption by Soda Lime in a Closed System. *Brit. J. Anaesth.*, **28**, 13.

Mousel, L. H., Weiss, W. A., and Gilliom, L. A. (1946). A Clinical Study of Carbon Dioxide Absorption during Anaesthesia. *Anesthesiology*, **7**, 375.

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THE EFFECT ON THE RESPIRATION OF THIALBARBITONE AND THIOPENTONE

BY

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THIALBARBITONE sodium (Kemithal) is now widely employed in clinical anaesthesia and among the several published reports it has been specially advocated in anaesthesia for paediatric operations (Stephen and Slater, 1946), Caesarean section (Gray, 1947), and for thoracic surgery (Halton, 1946). Thialbarbitone was synthesized in 1938 by Carrington and investigated pharmacologically by Carrington and Raventos (1946). Since the publication of the original investigations several workers have reported that in equivalent dosage it depresses the respiration less than thiopentone sodium. A search of the literature fails to reveal upon what clinical experimental evidence this opinion is based. The present work was accordingly undertaken to compare the effects on the respiration of thialbarbitone sodium and thiopentone sodium given in equivalent dosage under standard clinical conditions. A ratio of 2:1 with thiopentone was adopted because the majority of previous workers (Gordon and Gibbons, 1946; Stephen and Slater, 1946; Macintosh and Scott, 1946; Pellet, 1952) considered this to be the equipotent dosage and because this is the ratio recommended by the manufacturers.

Material and Method.

The investigation was carried out on 120 patients who were about to undergo surgical operation. Sixty received thialbarbitone and 60 thiopentone in fixed dose per weight on a completely unselected basis. (Some of the 60 thiopentone cases form part of another research undertaken under identical conditions (Swerdlow, 1957).) An age limit of 18–50 years was applied; all the subjects were in good general condition. The age, weight and sex distribution of the two series of subjects are shown in table I.

TABLE I

Distribution of patients

	Thiopentone series	Thialbarbitone series
Mean age (years)	32.3	32.7
Mean weight (kg)	59.8	61.9
Min. weight (kg)	41	44
Max. weight (kg)	77	81
No. of males	28	26
No. of females	32	34

All patients had been premedicated with morphine 11 mg and atropine 0.64 mg given s.c. 45 minutes before testing began; this combination has been shown elsewhere (Swerdlow and Newman, 1957) to be the least depressant to the respiration.

On arrival in the anaesthetic room the patient's mouth and pharynx were sprayed with 2 per cent amethocaine solution. The respiratory measurements were carried out in the anaesthetic room and were entirely completed before anaesthesia proper, and the operation, commenced. Respiratory volume was measured with a Bennett respiration meter inserted into the expiratory side of a Coxeter Mushin circle absorber. This meter is claimed to be accurate to within 5 per cent and under the conditions of the present work offers a resistance of less than $\frac{1}{4}$ cm of water. It allows of measurement to the nearest 25 ml. (A more detailed account of the experimental technique will be found under the reference to Swerdlow, 1957).

Control readings of the respiratory rate and minute volume were first taken. The patients were then treated as follows.

Thiopentone Series.

At the time "zero" 8 mg/kg sodium thiopentone in 5 per cent solution was injected into an

arm vein in 45 seconds. A mask was then applied to the face and nitrous oxide and oxygen, in 3:1 ratio, were administered via the closed circuit throughout the test. A Guedel's airway was inserted if necessary.

Three, five and nine minutes after "zero" the respiration rate and volume were measured for 1 minute. Ten minutes after "zero" 30 of the patients received a second injection of thiopentone, this supplementary dose being 2 mg/kg body weight. Further readings of the respiratory rate and minute volume were taken at the 13th and 15th minutes.

Thialbarbitone Series.

The procedure was identical with that used for the thiopentone series except that the induction dose of thialbarbitone was 16 mg/kg body weight and the supplementary dose was 4 mg/kg—both administered intravenously in 10 per cent solution.

A temporary apnoea (or gross hypopnoea) followed the initial dose of thiobarbiturate, and the lungs were artificially inflated for a short time. In no case was apnoea still present at the time of the 3-minute reading nor did it supervene at any later time.

RESULTS

The effects of the two thiobarbiturates will be detailed and compared under the headings of the respiratory functions affected.

Respiratory Rate.

Neither barbiturate had much effect on the respiration rate, which remained fairly steady throughout, both in those who received only one dose and in those who received a second dose (see table II).

Minute Volume.

The minute volume changes in the two series of patients are shown in table III. The control figures are closely similar in the average over the two series of 60 patients. It is clear that at 3, 5 and 9 minutes after the initial dose of thiobarbiturate there was no appreciable difference in the mean minute volumes in the two series. Both drugs caused a marked fall in the minute volume by the 3rd minute after injection and after both drugs the minute volume had returned to about control level by the 5th minute and remained at this level at the end of the 9th minute.

The supplementary injection of thiopentone caused a 23 per cent reduction in minute volume after 3 minutes while the supplementary dose of

TABLE II
Respiratory rate
(logarithmic averages)

Group	Effect of 1st injection (120 patients)				Effect of 2nd injection (60 patients)		
	Control	3 min	5 min	9 min	9 min	13 min	15 min
Thialbarbitone	16.7	16.4	16.8	16.1	16.4	16.6	16.3
Thiopentone	17.1	17.9	18.0	17.5	18.3	17.3	17.1
Ratio $\frac{\text{Thialbarbitone}}{\text{Thiopentone}}$	0.98	0.92	0.93	0.92	0.90	0.96	0.96
	Average standard deviation 3.1 per cent				Average standard deviation 4.4 per cent		

TABLE III
Minute volume (ml)
(logarithmic averages)

Group	Effect of 1st injection (120 patients)				Effect of 2nd injection (60 patients)		
	Control	3 min	5 min	9 min	9 min	13 min	15 min
Thialbarbitone	5843	4623	5813	5806	5897	5290	5676
Thiopentone	5615	4658	5708	5705	5597	4566	4935
Ratio $\frac{\text{Thialbarbitone}}{\text{Thiopentone}}$	1.04	0.99	1.02	1.02	1.05	1.16	1.15
	Average standard deviation 4.2 per cent				Average standard deviation 6.2 per cent		

thialbarbitone caused an 11 per cent depression of minute volume at the same time interval. At the 15th minute the subjects who had received thialbarbitone had recovered to 96.3 per cent of the 9-minute minute volume while the mean minute volume in the thiopentone group was only 88.2 per cent of the 9-minute control value. The depression of minute volume produced by thiopentone is significantly greater at 13 and 15 minutes than that produced by thialbarbitone; there is only a 1 in 40 probability that this apparent superiority of thialbarbitone is due to chance.

Tidal Volume.

Table IV shows that the initial dose of both thiobarbiturates caused, within 3 minutes, a fall in tidal volume in the order of 20 per cent. With both drugs the tidal volume had returned to around the control value by the 5th minute.

Three minutes after the second dose of thiopentone the tidal volume had fallen 21 per cent below the 9-minute value and at the 15th minute it was still 13 per cent below this value. At the corresponding times after thialbarbitone the tidal volume changes were −12 per cent and −3.6 per cent. The difference is statistically significant; there is a probability of 1 in 20 that the apparent superiority of thialbarbitone is due to chance.

Minute Alveolar Ventilation (M.A.V.).

In calculating the M.A.V. a dead space of 50 ml was assumed for the mask and connection piece and the patient's dead space was calculated from the formula: dead space = 1 ml per 1 lb body weight (Radford, 1955). Owing to wide individual variation in tidal volume subtraction of this calculated dead space occasionally gave a bizarre M.A.V., and logarithmic averages were therefore inappropriate. The arithmetic averages of the minute alveolar ventilation are given in table V. It will be seen that the M.A.V. follows the same general pattern as the minute and tidal volumes. The superiority of the second dose of thialbarbitone over that of thiopentone is numerically greater for M.A.V. than for tidal volume or minute volume. The difference between the effects of the second dose of the two drugs is statistically significant at the 13th and 15th minutes.

DISCUSSION

The introduction of the ultra-shortacting barbiturates inaugurated a new era in anaesthesia. Justifiably these agents were rapidly and universally adopted and today form an integral part of most general anaesthetic techniques as well as playing a supplementary role when regional methods are being employed. One of the less desirable features of the thiobarbiturates is their

TABLE IV
Tidal volume (ml)
(logarithmic averages)

Group	Effect of 1st injection (120 patients)				Effect of 2nd injection (60 patients)		
	Control	3 min	5 min	9 min	9 min	13 min	15 min
Thialbarbitone	351	281	346	361	359	320	348
Thiopentone	329	261	317	334	320	265	290
Ratio $\frac{\text{Thialbarbitone}}{\text{Thiopentone}}$	1.07	1.08	1.09	1.08	1.12	1.21	1.20

TABLE V
Minute alveolar ventilation (ml)
(arithmetic averages)

Group	Effect of 1st injection (120 patients)				Effect of 2nd injection (60 patients)		
	Control	3 min	5 min	9 min	9 min	13 min	15 min
Thialbarbitone	2827	1818	2862	2948	2904	2318	2721
Thiopentone	2671	1700	2610	2784	2616	1528	1946
Ratio $\frac{\text{Thialbarbitone}}{\text{Thiopentone}}$	1.06	1.07	1.10	1.06	1.11	1.52	1.40

depressant action on the respiration, an effect which is aggravated by other drugs employed in anaesthesia (Swerdlow, 1957). A thiobarbiturate which caused minimal respiratory depression would, all things being equal, be highly desirable in anaesthesia, particularly in techniques involving the use of repeated doses.

The evidence with regard to thialbarbitone is as yet incomplete. In the experimental animal Carrington and Raventos (1946) found that in equivalent dosage thialbarbitone causes about half as much respiratory depression as thiopentone. Bizard, Vanlerenberghe and Robelet (1952), on the other hand, report that in dogs 1.5 cg/kg thiopentone depressed the excitability of the respiratory centre to CO_2 for 3 hours whereas 3 cg/kg thialbarbitone depressed the centre for 6 hours. Dundee (1955) measured the duration of narcosis in the rat after equivalent doses of thiopentone and thialbarbitone and found that the two drugs had similar cumulative actions. Reynolds (1939) and Wyngarden et al. (1949) showed that repeated doses of thiopentone have a progressively longer effect. Raventos (1956), however, finds that on repeated administration successive doses of thialbarbitone do not augment as much as thiopentone.

In man the respiratory effects of the two drugs have not hitherto been compared quantitatively, although some workers have formed a clinical impression that thialbarbitone is less depressant than thiopentone. Way (1951) found that after 5 ml 5 per cent thiopentone injected in 15 seconds there was 33.7 seconds apnoea, while after the same volume of 10 per cent thialbarbitone given at the same speed the mean apnoeic period was 25.1 seconds.

It is clear from the present findings that, in a ratio of 2:1, single doses of thialbarbitone and thiopentone cause similar respiratory depression. It would seem, therefore, that the impression gained by earlier workers was based on observation of the effects of repeated injections of these drugs.

[It would obviously be of considerable interest to know the effect of multiple supplementary doses of these thiobarbiturates. Such an investigation has been commenced and the data so far obtained, although inadequate for publication, appear to confirm the above conclusions.]

SUMMARY

(1) Sixty patients received a standard dose per body weight of thiopentone and 60 were given a dose of thialbarbitone in a ratio of 1:2. Minute and respiratory rate were measured before and 3, 5 and 9 minutes after the injection. Thirty patients of each group were given a second injection of the respective drug at the 10th minute. Readings of the respiratory rate and minute volume were taken 3 and 5 minutes after the second dose.

(2) The initial dose of both thiobarbiturates caused a similar fall in minute volume, tidal volume, and minute alveolar ventilation.

(3) The second dose of thialbarbitone caused a significantly smaller depression of minute volume, tidal volume and minute alveolar ventilation than did the second dose of thiopentone.

ACKNOWLEDGMENTS

My thanks are due to Dr. O. L. Davies, Statistician, Pharmaceutical Division, I.C.I., for carrying out the statistical analysis of the results.

REFERENCES

Bizard, G., Vanlerenberghe, J., and Robelet, A. (1952). *C.R. Soc. Biol.*, **146**, 1121.

Carrington, H. C., and Raventos, J. (1946). *Brit. J. Pharmacol.*, **1**, 215.

Dundee, J. W. (1955). *Anaesthesia*, **10**, 391.

Gordon, R. A., and Gibbons, A. K. (1946). *Lancet*, **1**, 768.

Gray, T. C. (1947). *Brit. med. J.*, **1**, 444.

Halton, J. (1946). *Lancet*, **1**, 771.

Macintosh, R. R., and Scott, R. D. (1946). *Lancet*, **1**, 767.

Pellet, C. (1952). *Thèse Doc. Med.* (*Bordeaux*).

Radford, E. P. (1955). *J. Appl. Physiol.*, **7**, 451.

Raventos, J. (1956). Personal communication, unpublished work.

Reynolds, C. (1939). *Curr. Res. Anesth.*, **18**, 270.

Stephen, C. R., and Slater, H. M. (1951). *Anesthesiology*, **12**, 135.

Swerdlow, M. (1957). *Anaesthesia* (in press).

—— Newman, J. (1957). *Brit. J. Anaesth.* (in press).

Way, G. L. (1951). *Praxis*, No. 14, 283–284.

Wyngarden, J. B., Woods, L. A., and Seevers, M. H. (1949). *J. Pharmacol.*, **95**, 322.

Brit. J. Anaesth. (1957), **29**, 25

THE ANAESTHETIC MANAGEMENT OF A SEVERELY BURNT CHILD*

BY

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EARLY in January of 1956 an all too common accident occurred; a small child aged five years caught her nightdress on an electric fire and as a result she sustained severe burns. Within half an hour she was admitted to hospital in an extremely shocked condition. Immediately an intravenous drip of plasma was set up by means of a cut down drip. As sedation 7.5 mg of morphine was given into the drip. Penicillin therapy was started.

In assessing the severity of the burns Matthews (1952) has emphasized the following factors:

Extent. The systemic reaction which is to be expected is proportional to the size of the burn. This when expressed as a percentage of the total surface area is of assistance in calculating the amount of fluid required to combat oligaemic shock. Wallace's (1951) "Rules of Nine" for estimating the area of burn is of great practical help in this matter (fig. 1).

Depth. It is now more usual to stress only two degrees of burning, namely:

(*a*) Partial skin destruction,

(*b*) Total skin destruction,

the original classical six degrees of Dupuytren (1832) having been largely abandoned.

Site. McIndoe (1940) has pointed out that although the area of burn may only be slight in certain areas, it may be followed by crippling disabilities and thus the burn should be regarded as serious.

Time since burning is of importance. Delay in treating a burnt patient may have serious consequences and secondary infection may supervene.

Examination of this little girl revealed that more than 50 per cent of the body surface was burnt with total skin destruction comprising:

(1) Neck and under surface of jaw.

(2) The whole of the back and front of the trunk.

(3) Both arms and axillae.

(4) Both thighs.

The next procedure was to catheterize the the patient and begin an input and output fluid chart. The fluid intake was adjusted by mouth and the intravenous route to (1) replace fluid lost from the burns, and (2) to try and maintain a urinary output of 30 ml per hour.

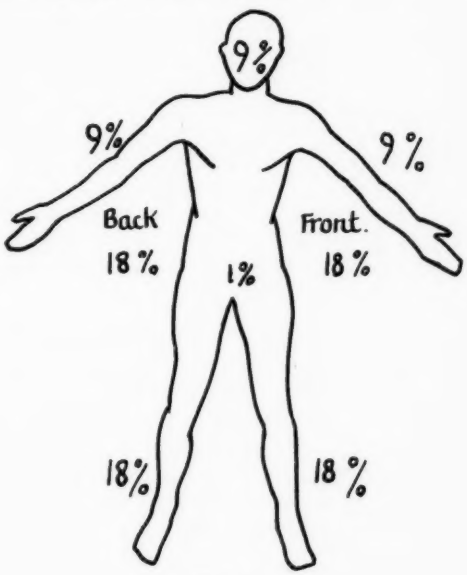

FIG. 1

To calculate the required amount of fluid it is suggested that 100 ml for every 1 per cent of the body surface burnt is required over 48 hours (Battle et al., 1954). It was therefore calculated that this patient required in the first 24 hours 2,400 ml plus 1,200 ml (insensible sweat loss). This was given in the ratio of half whole blood, quarter plasma, and a quarter saline, the whole blood to replace corpuscles damaged in the full thickness burns.

* Based on a Paper read to the Yorkshire Society of Anaesthetists.

The suggested rate of transfusion in these cases is calculated as follows:

The number of litres × 12 in 24 hours
equals the number of drops per minute.

On the next day the blood picture was investigated and it was found that the haemoglobin was 121 per cent, showing considerable evidence of haemoconcentration in spite of intravenous therapy. The blood urea was 40 mg per cent.

It was not until 7 days after admission, that her general condition warranted dressing and toilet of the burns under full general anaesthesia.

On the first occasion premedication consisted of 25 mg chlorpromazine and 90 mg of pentobarbitone, atropine being omitted on account of severe tachycardia.

In the anaesthetic room the respiratory rate was between 50 and 60 per minute. The patient was cyanosed and restless and it was clear that the respiratory passages were choked with secretions. In view of this a child's bronchoscope with suction catheters was kept ready on the trolley. A Cobb's adaptor was attached to the endotracheal tube to facilitate aspiration of secretions. In addition a tracheotomy set was at hand in case intubation proved impossible as a result of laryngeal distortion from the neck burns.

Induction was commenced with cyclopropane and oxygen and when the child was asleep a vein was sought and 20 mg of suxamethonium were injected. On insertion of the laryngoscope it was seen that marked flooding of the bronchial tree with purulent fluid had occurred. This was cleared by suction and after the insertion of an orotracheal tube (Portex No. 3) suction was continued through this. Anaesthesia was maintained with cyclopropane and oxygen using circle absorption. During this anaesthetic no sensitivity to suxamethonium was encountered, spontaneous respiration quickly returned, and recovery was rapid and uneventful.

Some three weeks later, using the same routine, toilet and débridement of the burns followed by application of homografts were carried out. Subsequently she was dressed weekly under light cyclopropane anaesthesia until the middle of February at which time it was evident that further skin coverage of the burnt areas was imperative. The patient's mother was then brought into hospital in order to obtain donor grafts which were to be used to cover the extensive raw areas.

Towards the end of February the vein problem had become very acute indeed and we had to resort to setting up a transfusion using the superficial temporal vein.

Subsequently the patient, showing gradual progress, has been anaesthetized twice a week until the present time (June 1956) comprising some 34 anaesthetics for dressings and at other suitable times for skin grafting.

In mid-March a prolonged response to suxamethonium was noted and this afforded some little anxiety as it was thought there might possibly be amyloid change in the liver. Since then gallamine triethiodide has been the relaxant of choice in a dose of approximately 20 mg to facilitate intubation if required.

DISCUSSION

The giving of repeated anaesthetics to small children is a commonplace experience for anaesthetists attached to a Plastic Unit. There are, however, few reports on such series.

Allen and Slocum (1952) have a series of 240 patients receiving a total of 1,400 anaesthetics. In a recent article, Wiznitzer and Neusman (1956) reported a case receiving 48 anaesthetics. Bachman (1949) reported a case receiving 23 anaesthetics.

Every anaesthetist realizes that small children generally dread anaesthetics. The question of retaining the child's confidence when some fifty anaesthetics may be required is indeed difficult. In this particular case venepuncture often proved impossible so that intravenous thiopentone was impracticable. The rectal route was precluded initially on account of extreme tenderness and oedema of the genital area and buttocks.

The anaesthetic care of this case illustrates some of the points mentioned by Shannon (1955). He states that:

(A) It is impossible to dogmatize on the best anaesthetic.
(B) A high concentration of oxygen is necessary to satisfy the metabolic demands of the child.
(C) Rapid recovery to allow full and early resumption of dietetic regime is required.

Cyclopropane is well suited to meet these demands of the child as it can be given with high

concentrations of oxygen. Control of the depth of anaesthesia is easier by the inhalational route as venepuncture may not be feasible. Cyclopropane is excreted unchanged from the body and recovery is rapid. The method of administration is by circle absorption in children over three years. The very young are better anaesthetized using to and fro absorption.

Despite the application of a mask the child has remained remarkably co-operative and will willingly breathe from the mask at each induction.

SUMMARY

(1) A method of anaesthetizing a severely burnt child is described.

(2) The assessment of the severity of a burn is discussed.

(3) The subsequent anaesthetic management and the problem of multiple anaesthetics is commented upon.

ACKNOWLEDGMENTS

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REFERENCES

Allen, C. R., and Slocum, H. C. (1952). The Functions of the Anaesthesiologist in the Management of the Patient with Extensive Burns. *Anesthesiology*, **13**, 65.

Bachman, C. W. (1949). Pentothal Sodium Requirements in Man: Report of a Case. *Anesthesiology*, **10**, 111.

Battle, R. J. V., Clarkson, P., Rainford, M., Osborne, R., and Wallace, A. B. (1954). Fluid Replacement in Burned Patients. *Lancet*, **1**, 98.

Dupuytren, G. (1832). *Leçon Orales de Clinique Chirurgicale.*, **1**, 413.

Matthews, D. N. (1952). Burns. *Ann. roy. Coll. Surg.*, **10**, 114.

McIndoe, A. H. (1940). Functional Aspect of Burn Therapy. *Proc. roy. Soc. Med.*, **34**, 56.

Shannon, D. W. (1955). An Anaesthetist Looks at a Burnt Child. *Lancet*, **1**, 111.

Wallace, A. B. (1951). The Exposive Treatment of Burns. *Lancet*, **1**, 501.

Wiznitzer, Th., and Newman, Z. (1956). Multiple General Anaesthesia. A Case of Severe Burns. *Anaesthesia*, **11**, 241.

BOOK REVIEW *continued from page* 11

oxygen as an anaesthetic agent is discussed at length and the wisdom of its unassisted use in the dental chair is questioned. The value of premedicant drugs and adjuvants to increase the safety of the anaesthesia is described, while the hazards of thiopentone in dental anaesthesia are discussed. The changing concepts of the use of nitrous oxide already make this section somewhat out of date, in view of several recent publications on the satisfactory use of nitrous oxide without hypoxia.

Local and regional anaesthesia (key number 352, pages 165–168) are discussed in greater detail than general anaesthesia. With the acceptance of the B.P. name of lignocaine, it is out of keeping with the general standard of the book to find a section on " Xylocaine ". Even more surprising is the use of the words Novocaine and Coramine. In this country, at least one would not call the prophylactic use of dihydroergotamine before the injection of large quantities of a local anaesthetic containing adrenaline an accepted practice, however desirable this may be, yet this is discussed at some length. Efocaine appears to have been given more publicity than clinical results seem to warrant, and although a warning is given that it should be used with much greater caution than heretofore, there are many who consider that this is an understatement and that it is not yet an agent of " proved value ".

Apart from the section on anaesthetic drugs, the anaesthetist will find in this volume a comprehensive review of basic experimental and clinical work on ACTH, cortisone and related substances (pages 6 to 24), which in conjunction with a similar section referred to above should give a sound background to the use of these drugs. In the section on heart diseases there is also much information which can benefit the anaesthetist in his pre-operative dealings with such cases and in the operating theatre.

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CHLORPROMAZINE AS AN ADJUVANT IN THE RELIEF OF CHRONIC PAIN

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> "We must still suffer pains which seem to have no purpose but remind us of our frailty."
> (Adrian, 1947)

MUCH has been done in recent years to ascertain the nature of pain and improve the methods available for its treatment. New and more effective analgesics have been synthesized to overcome the disadvantages of the opiates, and these have been combined with drugs which antagonize their depressant effects on respiration (Cullen and Santos, 1954). Bonica (1953) has described the indications for, and techniques of, nerve blocks in great detail. Beecher (1951) has stressed the importance of the mental and physical comfort of the patient in the management of pain.

Despite these advances there are still many problems to be solved. One of the physician's greatest difficulties is the treatment of the patient who has become resistant to those analgesics which offer the only hope of effective relief of pain. This group includes many persons in the terminal stages of malignant disease.

From a consideration of the properties of chlorpromazine this drug would seem to offer some hope in such patients. It potentiates the analgesic action of morphine, pethidine, acetylsalicylic acid and phenacetin (Courvoiser et al., 1953); during anaesthesia it potentiates the effects of pethidine (Laborit et al., 1952); and its use after operation reduces the requirements of postoperative analgesics (Forster et al., 1952). It has a mild sedative action and in large doses it is reputed to have a central action, which has been termed "pharmacological frontal leucotomy" (Terzain, 1952).

Chlorpromazine also has other actions which may be beneficial in some of the conditions which are associated with chronic pain. It is a powerful anti-emetic drug, and has been used for the treatment of vomiting from a variety of causes (Glaviano and Wang, 1955; Moyer et al., 1954), including uraemia (Friend and Cummins, 1954), radiation therapy (Marks, 1954), and malignant disease (Homburger and Smithy, 1954). Aivazian (1955) and Freidgood and Ripstein (1955a) have found chlorpromazine of value in the withdrawal of drugs of addiction, while Cummins and Friend (1954), Mitchell (1955) and Fazekas et al. (1955) have also shown its beneficial action in alcoholism. Freidgood and Ripstein (1955b) have also found that chlorpromazine relieves intractable hiccough in a large percentage of patients.

This report deals with the use of oral chlorpromazine as an adjuvant in the relief of pain, and analyzes in detail the results obtained in 76 patients treated over a period of 30 months. The findings are later compared with those in a further 48 subjects who were not studied in so great detail or else treated by other practitioners. A final assessment of this aspect of the use of chlorpromazine is based on experience with 124 cases, and suggestions are made as to its place in the treatment of pain.

CLINICAL DATA

The causes of pain in the 76 patients, who form the main part of this study, are shown in table I. The pain in these subjects was either not amenable to surgical treatment or nerve blocks, or else the patients were unwilling to undergo such treatment. When first seen, many of these patients were receiving inadequate relief from moderate doses of analgesics. At the beginning of the series, chlorpromazine was used only in patients with malignant disease. Other types of pain were treated later but, for reasons to be discussed, towards the end chlorpromazine was again reserved for patients with pain due to neoplasms.

The ages of the 76 cases ranged from 33 to 89 years, with an average age of 59.

TABLE I
Causes of pain.

Malignant Disease		38 patients
Gastrointestinal tract	14	
Gynaecological	6	
Breast	6	
Tongue	4	
Prostate	3	
Upper respiratory tract	2	
Lower respiratory tract	2	
Spinal cord	1	
"Nerve" Pains		25 patients
Trigeminal neuralgia	12	
Involvement in scar tissue	8	
Post-herpetic neuralgia	4	
Causalgia	1	
Osteoarthritis		6 patients
Others		7 patients
Facial tic	2	
Fibrositis	2	
? Psychogenic	3	
Total		76 patients

METHOD OF TREATMENT

One-sixth of the patients were first treated in hospital and seen thereafter at frequent intervals as outpatients. With the exception of three subjects, who were hospitalized throughout the period of observation, the remainder were seen at a weekly outpatient clinic. Of necessity, a few patients were treated in their homes when the terminal stages of malignant disease made it impossible for them to attend hospital.

As far as possible all analgesics were given by mouth and the patients were kept ambulant.

The regime for treatment with chlorpromazine varied from case to case, depending on the severity and the cause of the pain, the nature and quantity of the analgesics already being administered and the beneficial effects produced by these. Another important factor was whether patients were in hospital or attending as outpatients. In general, the principles of treatment were as follows:

(1) If the patients were suffering severe pain and already receiving ineffective relief from analgesics, chlorpromazine was added to these drugs. Where this increased the efficacy of the treatment, an attempt was made to reduce the dose of analgesics. Failure to obtain a beneficial effect with daily doses of 250 mg chlorpromazine and increasing amounts of analgesics was taken as an indication to change to another analgesic.

(2) In cases with severe pain, not already receiving any drugs, a trial was first given to analgesics alone, and the degree of pain relief assessed before adding chlorpromazine.

(3) With moderately severe untreated pain, a trial was sometimes given to chlorpromazine alone for several weeks.

(4) The initial daily dose of chlorpromazine was 25 mg, which was gradually increased to 25 mg three times daily over the first week. Where necessary, this was increased to 25 mg four-hourly during the day (125 mg daily), 50 mg three or four times daily (150–200 mg daily), or even to 50 mg four-hourly during the day (250 mg daily) until a beneficial effect was obtained. The latter dose was never exceeded in outpatients.

If, at any time, the patient, whose pain was amenable to relief with surgical or nerve block therapy, decided to have such treatment, this was carried out and the chlorpromazine and analgesics were gradually stopped. In no case was there difficulty with the withdrawal of analgesics.

DURATION OF TREATMENT

Table II shows the duration of treatment and the reasons for its cessation. The high mortality occurred in patients with malignant disease and there was no reason to suspect that this was influenced in any way by the use of chlorpromazine. The patients who were relieved by other procedures were mostly those suffering from trigeminal neuralgia or those in whom the pain was due to involvement of peripheral nerves in scar tissue.

ASSESSMENT OF RESULTS

Holmes (1947) has pointed out that pain is so wholly subjective that an accurate estimate of its severity is always difficult. In this series, in assessing the effects of chlorpromazine, reliance was placed on the patients' statements and those of relatives or nursing staff. It was difficult to make allowance for increasing severity of pain, such as would occur with increasing size of a tumour, or with metastatic spread during the period of observation.

The following classification of results is based on that described by Beecher (1951).

++ Good relief of pain. Patients were more comfortable; benefit was maintained as

TABLE II

Duration of and reasons for cessation of treatment in 76 cases.

Duration of treatment	No. of cases	Reason for cessation of treatment					
		Insufficient benefit	Death of patient	Side effects	Pain relieved by other means	Lost touch with patient	Still continuing
1 week	12	3	1	2	6	–	–
1–2 weeks	14	3	6	–	2	2	1
2–4 weeks	14	5	6	–	1	2	–
1–2 months	13	–	6	–	3	3	1
2–4 months	10	–	6	–	3	1	–
4–6 months	6	–	3	–	–	2	1
6 months +	7	–	5	–	–	–	2
Total	76	11	33	2	15	10	5

long as desired, even if increasing doses of drugs were required.

\+ Moderate benefit. This includes cases where less pain was experienced but with no increase in comfort, patients in whom comfort was increased with only moderate diminution of pain, and those in whom there was at first good relief of pain which, however, was not maintained.

– Negligible or no relief of pain with no increase in the comfort of the patient.

L Patients who showed a " leucotomy-like " effect of indifference to pain or indifference to the cause of pain (Dynes and Popper, 1949).

Patients with whom contact was lost were assessed as having the degree of pain relief present when last seen. Any patients about whom a definite opinion could not be made were excluded from the series.

RESULTS

These are summarized in table III. It is obvious that chlorpromazine alone possesses little analgesic power of its own, as the percentage of patients (27 per cent) who benefited when it was used alone was no higher than one would expect from the use of a placebo. The best results were obtained in patients with pain due to malignant disease, by combining chlorpromazine with analgesics, 89 per cent of such cases receiving some benefit. Less than half the percentage of patients with nerve pains obtained good relief as compared with the previous group.

An appreciable number of these patients who were, at first, unwilling to undergo any form of nerve-block treatment, requested that this be carried out after they had received chlorpromazine for several weeks.

The results were disappointing in cases with arthritis, and the highest number of undesirable

TABLE III

Effects of chlorpromazine alone, or in combination with analgesics in 76 patients. For classification of results, see text.

Cause of pain	Total number of cases	Chlorpromazine alone					Chlorpromazine + analgesic				
		No. of cases	Result				No. of cases	Result			
			++	+	–	L		++	+	–	L
Neoplasms	38	6	0	2	4	1	36	21	11	4	7
Nerve	25	16	1	3	12	0	22	6	9	7	2
Arthritis	6	3	0	0	3	0	5	1	2	2	0
Others	7	4	1	1	2	2	4	2	0	2	1
Total	76	29	2	6	21	3	67	30	22	15	10

side effects occurred in these subjects. In the last group the only good results were in three patients with pain which was thought to be psychogenic in origin.

Contrary to expectations the leucotomy-like effect was not marked with the doses of chlorpromazine used. It occurred in one-fifth of the cases with malignant disease, and was probably the main reason for the successful treatment of patients with psychogenic pain.

Table IV related the degree of pain relief with the analgesic used, irrespective of the nature of the pain. Best results were obtained with levorphan (Dromoran, 1.5 mg tablets) and papaveretum (Omnopon, 10 mg tablets), but the soporific effects of the latter drug were a disadvantage when given to outpatients. Tabs. codeine. co. (N.F.), combined with chlorpromazine, gave good results in patients with moderately severe pain and often proved more effective and produced less side effects than the more powerful analgesics.

TABLE IV

Beneficial effects of chlorpromazine therapy, related to analgesics used, irrespective of the nature of the pain.

Analgesic	No. of cases	Degree of benefit ++	+	−	L
Tabs. codeine co.	28	9	14	5	0
Levorphan	25	15	6	4	3
Aspirin and similar drugs	11	2	8	1	0
Pethidine	10	5	2	3	3
Papaveretum	8	5	1	2	4
Amidone	5	3	0	2	2
Phenadoxone	5	0	1	4	0

Side effects

Chlorpromazine is a drug with many actions other than potentiating analgesics, and side effects during its use were not unexpected. These are listed in table V. It can be seen that about one-third of the patients complained of no undesirable effects from chlorpromazine. In only two patients was it necessary to discontinue treatment.

Drowsiness occurred frequently at the beginning of treatment but with two exceptions, tolerance rapidly developed to the soporific effects of chlorpromazine. This is in agreement with the experience of other workers. Dryness of the mouth diminished in intensity as treatment continued, but seldom disappeared completely. This also applied to anorexia. With the exception of one patient, hypotension was not a troublesome complication in this series, and it could usually be avoided by instructing the patients to lie down if they felt faint.

TABLE V

Complications of chlorpromazine therapy in 76 patients.

Side effects	Number of cases	Side effects	Number of cases
Drowsiness		Jaundice	1
temporary	33	Dryness of mouth	16
prolonged	2	Loss of appetite	14
Pyrexia		Drugged feeling	6
temporary	10	Headache	5
Constipation	5	Mental depression	3
Faintness		Palpitations	5
temporary	5	Visual disturbances★	3
prolonged★	1	Nausea	3
Itching	3		

Number of side effects complained of

None	24	patients
1	25	,,
2	12	,,
3	8	,,
4 or more	7	,,

★ Side effects were of sufficient severity to necessitate discontinuance of chlorpromazine in two of these patients.

Visual disturbances, consisting of diplopia and inability to focus, were very severe in one patient but disappeared soon after stopping chlorpromazine.

Pyrexia occurred during the second week of chlorpromazine therapy in 10 patients. It was sometimes associated with an influenza-like attack, headache and nausea or itching, and one subject subsequently became jaundiced. Liver function tests in this patient showed an elevation of the serum bilirubin and alkaline phosphatase levels, but there was no abnormality in the flocculation tests or serum cholinesterase levels to suggest the occurrence of parenchymatous liver damage. Chlorpromazine was stopped four days after the onset of jaundice. Resumption of the treatment, when the jaundice had cleared, produced no ill effects during a ten-week period.

Other cases.

The results obtained with chlorpromazine, with or without analgesics, in a further series of 48 patients, treated on the same lines as above, are given in table VI. In this series the results of the treatment were assessed by other practitioners who were in closer contact with the patients.

Sadove and his colleagues (1954, 1955) found that the combination of chlorpromazine with drugs which had previously proved ineffective for relieving pain, proved beneficial in 22 out of 28 cases. Some patients could be made more comfortable with a lower dosage, or with less powerful analgesics than they had previously required.

TABLE VI

Results of the use of chlorpromazine alone, or in combination with analgesics, in 48 patients treated and assessed mostly by other practitioners.

Cause of pain	Total number of cases	Chlorpromazine alone					Chlorpromazine + Analgesic				
		No. of cases	Result				No. of cases	Result			
			++	+	−	L		++	+	−	L
Neoplasms	19	5	0	2	3	4	19	9	7	3	7
Nerve	18	13	0	1	12	0	14	6	4	4	1
Arthritis	4	3	0	0	3	0	3	2	0	1	0
Others	7	7	0	1	6	3					
Total	48	28	0	4	24	7	36	17	11	8	8

It can be seen that the findings are essentially the same as in table III: 84 per cent of patients with malignant disease benefited from the use of chlorpromazine, as compared with 89 per cent in the previous series. One difference was the higher incidence of the " leucotomy-like " effect of chlorpromazine recorded in table VI. This is probably due to a difference in interpretation of the presence of this effect by different observers.

DISCUSSION

This report is not presented as conclusive evidence of the value of chlorpromazine as an adjuvant in the relief of pain. Ideally, the nature of the drugs administered should not have been known to the person who was assessing the effects of the treatment, and placebos should have been periodically substituted for chlorpromazine. It would not always have been possible to carry out the first recommendations, and with the severity of the pain suffered by many of the patients it was felt that the use of placebos was not justifiable.

However, the findings are in agreement with those of other workers in the same field. Vialard (1953) found that an infusion of pethidine and chlorpromazine eased pain in two patients who were resistant to the analgesic action of opiates. Howell, Harth and Dietrich (1954) have used chlorpromazine in geriatrics, and found it of value in 18 out of 19 patients who were suffering from severe pain. Good results have also been claimed by Lucas et al. (1954) in 32 cancer patients, who were suffering from nausea and vomiting or from pain which could not be controlled by reasonable doses of analgesics.

Two-thirds of the 76 patients, which formed the main part of this study, exhibited undesirable effects from the use of chlorpromazine. In only two patients was it necessary to discontinue treatment because of side effects. This is a lower incidence than reported by some workers who have used chlorpromazine in psychiatry. In the latter field much higher doses (up to 700–800 mg daily) are frequently used.

The occurrence of any of the complications in table V may be a deterrent to the use of chlorpromazine, except in patients with severe pain, but with reasonable caution they will not endanger life. Attention must be drawn to the 13 per cent incidence of temporary pyrexia which was accompanied by nausea in 4 per cent of cases and followed by jaundice in one patient. Most of the instances of jaundice reported after the use of chlorpromazine have been ushered in by an influenza-like attack. The mechanism of this

jaundice is not fully understood. Initially, at least, there appears to be little hepatocellular damage, but rather a blocking of the finer bile canaliculi.

Following the occurrence of jaundice in the one patient in this series, liver function tests were performed in sixteen patients who received between 1.5 and 24 g chlorpromazine over periods varying from 3 to 33 weeks. They will be reported elsewhere in detail. One patient showed an elevation of the serum bilirubin and alkaline phosphatase levels, which were associated with fever and nausea, but with no clinical detectable jaundice. In three cases there was a possibility of parenchymatous liver damage, as shown by the sensitive serum cholinesterase test. The report will review almost 6,000 reported long-term administrations of chlorpromazine and reveal a 1 per cent incidence of jaundice. There was a fatal outcome in four patients out of 92 reported cases of jaundice and the remarkably high figure of 13 per cent of cases underwent unnecessary laparotomy for obstructive jaundice.

It would appear inadvisable to administer chlorpromazine for long periods without frequent blood analyses for evidence of obstructive jaundice. An annotation in the *Lancet* (1955) pointed out that as the effects of chlorpromazine on the liver " are usually heralded by pyrexia, the risks are diminished if patients are instructed to stop taking the drug if the temperature rises." However, this advice was taken by Stacey et al. (1955) and two out of five subjects developed jaundice six or seven days later.

The prolonged use of chlorpromazine also carries the risk of agranulocytosis. Five out of ten reported cases ended fatally (Boardman, 1954; Giacobini and Lassenius, 1954; Lomas, 1954; Boleman, 1955; Goldman, 1955; Hodges and La Zerte, 1955; Moyer, 1955; Prokopowycz, 1955; Tasker, 1955). The significance of this complication was not realized until near the end of the present study, and except for the last eight patients, routine blood examinations were not carried out. These tests revealed no abnormality.

It is recommended that a careful watch be kept on the blood picture of patients undergoing this treatment, and that chlorpromazine be stopped, if there is any tendency to leucopenia.

In assessing the possible use of this drug, one must consider these results in light of the above discussion on its toxic effects. In pain due to malignant disease, 88 per cent of all patients benefited from the treatment and over half of these cases obtained good relief from pain. It is felt that since other forms of treatment offer little hope of relief for most of these patients, the risks associated with the prolonged use of chlorpromazine are justified. The results of treatment with chlorpromazine were not as good in the other types of pain and one must consider whether the chances of a beneficial outcome are such as to outweigh any dangers from the therapy.

SUMMARY

The effects of oral chlorpromazine as an adjuvant in the relief of pain have been studied in 76 patients. Very good results were obtained in subjects with malignant disease, but not so good results in other types of pain.

These findings were similar to those obtained in 48 similar patients, where the effects of the treatment were assessed by other practitioners. Best results were obtained with a combination of chlorpromazine and levorphan.

Side effects occurred in two-thirds of the patients, but only necessitated stopping the chlorpromazine in two subjects.

The occurrence of an influenza-like attack, followed by jaundice was the most serious complication encountered in this study.

It is suggested that serum bilirubin and alkaline phosphatase determinations and leucocyte counts be carried out at frequent intervals in patients who are having prolonged treatment with chlorpromazine.

The dangers associated with the use of chlorpromazine do not appear to be sufficiently great to preclude its use in patients suffering pain due to malignant disease. In other conditions one must assess whether the benefits likely to be obtained from the use of chlorpromazine are such as to outweigh the side effects associated with its use.

REFERENCES

Adrian, E. D. (1947). The Physiology of Pain. *Practitioner*, **158**, 76.

Aivazian, G. H. (1955). Chlorpromazine in the Withdrawal of Habit Forming Drugs in Addicts. *Dis. nerv. syst.*, **16**, 57.

Beecher, H. K. (1951). Pain and Some Factors that Modify It. *Anesthesiology*, **12**, 633.

Boardman, R. H. (1954). Fatal case of Toxic Hepatitis Implicating Chlorpromazine. *Brit. med. J.*, **2**, 579.

Boleman, A. P. (1955). Agranulocytosis Associated with the Administration of Thorazine. *J. Amer. med. Ass.*, **157**, 364.

Bonica, J. J. (1953). *The Management of Pain*. Philadelphia: Lea and Febiger.

Courvoisier, S., Fournel, J., Ducrot, R., Kolsky, M., and Koetschet, P. (1953). Proprietes pharmacodynamiques de chlorhydrate de chloro-3(dimethylamino-3′ propyl)-10 phenothiazine (4,560 R.P.). Etudes experimentale d'un nouveau corps utilise dans l'anesthesie potentialisee et dans l'hibernation artificialle. *Arch. Internat. de Pharmacodyn. et de Therap.*, **92**, 305.

Cullen, S. C., and Santos, C. C. (1954). Analgesia for Chronic Pain Without Respiratory Depression. *Arch. Surg.*, **69**, 410.

Cummins, J. F., and Friend, D. G. (1954). The Use of Chlorpromazine in Chronic Alcoholics. *Amer. J. med. Sci.*, **227**, 561.

Dynes, J. B., and Popper, J. L. (1949). Lobotomy for Intractable Pain. *J. Amer. med. Ass.*, **140**, 15.

Fazekas, J. F., Shea, J., and Rea, E. (1949). Use of Chlorpromazine in the Management of Acute and Postalcoholic Pain. *Internat. rec. med.*, **168**, 333.

Forster, S., Forster, E., Maier, A., and Blum, H. (1952). Anesthesie potentialisee en chirurgie thoracique. *Anesth. et. Analg.*, **9**, 250.

Freidgood, C. E., and Ripstein, C. B. (1955a). Use of Chlorpromazine in the Withdrawal of Addicting Drugs. *New. Eng. J. med.*, **252**, 230.

—— —— (1955b). Use of Chlorpromazine in the Withdrawal of Addicting Drugs. *New. Engl. J. med.*, **252**, 230.

Friend, D. G., and Cummins, J. F. (1954). Use of Chlorpromazine in the Treatment of Nausea and Vomiting of Uraemia. *New. Eng. J. med.*, **250**, 997.

Giacobini, E., and Lessenius, B. (1954). Chlorpromazine Treatment; Side Effects and Complications. *Nord. med.*, **52**, 1693.

Glaviano, V. V., and Wang, S. G. (1955). Dual Mechanism of anti-emetic action of Chlorpromazine. *J. Pharmacol.*, **114**, 358.

Goldman, D. (1955). Treatment of Psychotic States with Chlorpromazine. *J. Amer. med. Ass.*, **157**, 1274.

Hodges, H. H., and La Zerte, G. D. (1955). Jaundice and Agranulocytosis following Chlorpromazine Therapy. *J. Amer. med. Ass.*, **158**, 114.

Holmes, G. (1947). Some Clinical Aspects of Pain. *Practitioner*, **158**, 165.

Homburger, F., and Smithy, G. (1954). Chlorpromazine in Patients with Nausea and Vomiting due to Advanced Cancer. *New. Eng. J. med.*, **251**, 820.

Howell, T. H., Harth, J. A. P., and Dietrich, M. (1954). The Use of Chlorpromazine in Geriatrics. *Practitioner*, **173**, 172.

Laborit, H., Huguenard, P., and Alluame, R. (1952). Un Nouveau Stabilisateur vegetatif (Le 4560 R.P.). *Presse med.*, **60**, 206.

Lancet (1955). Drugs in the Treatment of Depression. **1**, 1065.

Lomas, J. (1954). Chlorpromazine and Agranulocytosis. *Brit. med. J.*, **2**, 358.

Lucas, J., Albert, S. N., Bateman, J. C., and Klopp, C. T. (1954). Thorazine as an Aid in Management of Cancer Patients. *Proc. Amer. ass. Cancer. Res.*, **1**, 30.

Marks, J. H. (1954). Use of Chlorpromazine in Radiation Sickness and Nausea from other Causes. *New Eng. J. med.*, **250**, 999.

Mitchell, E. H. (1955). Chlorpromazine in the Treatment of Acute Alcoholism. *Amer. J. med. Sci.*, **229**, 363.

Moyer, J. H. (1955). Chlorpromazine in Internal Medicine. *Internat. rec. med.*, **168**, 333.

Moyer, J. H., Kent, N., Knight, R. W., Morris, G., Dizon, M., Rogers, S., and Spurr, C. (1954). Clinical studies of an Anti-emetic agent, Chlorpromazine. *Amer. J. Med. Sci.*, **228**, 174.

Prokopowycz, V. (1955). Agranulocytosis following the use of Chlorpromazine Therapy. *J. Amer. med. Ass.*, **157**, 909.

Sadove, M. S., and Balagot, R. C. (1955). The Value of Chlorpromazine in the management of Pain. *Internat. rec. med.*, **168**, 346.

—— Levin, M. J., Rose, R. F., Schwartz, L., and Witt, F. W. (1954). Chlorpromazine and Narcotics in the Management of Pain of Malignant Lesions. *J. Amer. med. Ass.*, **155**, 636.

Stacey, C. H., Azema, H., Huestis, D. W., Howlett, J. G., and Hoffman, M. M. (1955). Jaundice Occurring during the Administration of Chlorpromazine. *Canad. med. Ass. J.*, **73**, 386.

Tasker, J. R. (1955). Fatal Agranulocytosis during Treatment with Chlorpromazine. *Brit. med. J.*, **1**, 950.

Terzain, H. (1952). Studio Elettroencefalografico dell'azione centrale del Largactil (4560R.P.). *Rass. neurol. veg.*, **4**, 211.

Vialard, C. (1953). Note sur l'utilisation du Largactil (4560 R.P.) comme potentialisateur de medicamentes analgesiques chez les cancereux douloureux resistants aux opiaces. *Anesth. et Analg.* **10**, 216.

Brit J. Anaesth. (1957), **29**, 35

THIOPENTONE IN DYSTROPHIA MYOTONICA

BY

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INTRODUCTION

DYSTROPHIA MYOTONICA (myotonia atrophica) is an hereditary familial disease with features intermediate between the myotonias and myopathies. It is transmitted as a simple dominant, and the onset of the disease in the children is at an earlier age than in the parent, until, after a generation in which the onset occurs before sexual maturity, it ceases to appear in that family. Males are affected more often than females, and the disease is generally latent until early adult life. The first symptom is usually a difficulty in relaxing the grip, and myotonic phenomena often develop in other muscles, so that, for example, a smile may be slow to disappear. The lower limbs are rarely affected. Exposure to cold aggravates the myotonia, as does acetylcholine, neostigmine and potassium. There is concurrent progressive muscular weakness and wasting, but the most conspicuous myotonia often occurs in muscles free from wasting, and conversely wasted muscle may not be myotonic.

Associated with the disease are various signs of premature senility, such as testicular or ovarian atrophy, frontal baldness, and mild euphoric dementia; and at least half the cases develop senile cataracts. Degeneration of various endocrine glands has occasionally been found, particularly the anterior pituitary, the thyroid, and the adrenal cortex, and thyroid adenomas and diabetes mellitus may also occur. Such metabolic changes as have been found are similar to those in other muscular dystrophies; the most notable is a disorder of creatine metabolism.

Creatine (Wright, 1952), which is synthesized in the liver, and is taken up from the blood by the muscles as needed, is stored in normal resting muscle mainly as creatine phosphate, the phosphate group being linked to creatine by a high-energy phosphate bond; it is formed by the reaction of creatine with adenosine triphosphate, and this reaction is reversible. Creatine phosphate can normally be stored in muscle, and its high-energy bonds are available for the rapid resynthesis of adenosine triphosphate, which is required for muscular work, from adenosine diphosphate. Creatine is not normally found in the urine except in children, but, in addition to certain other conditions, it may appear in the presence of pathological states of muscle, notably the myopathies, because of the poor ability of the diseased muscle to store creatine.

CASE REPORT

The patient, a male, aged 50, weight 10 st. 3 lb., was admitted under the care of Mr. J. Gibson Moore for the removal of a cataract from the left eye. He had been in Chase Farm Hospital fifteen years before with staphylococcal septicaemia, and in 1946 a cataract was removed from his right eye under local anaesthesia at another hospital; he was employed in the making of television tubes, and, unaware of his disease, and not conscious of any disability, he lived a normal active life. Routine pre-anaesthetic examination revealed no obvious abnormality. He received papaveretum ½ grain (20 mg), hyoscine 1/150 grain (0.45 mg) one hour before operation; and anaesthesia was induced with thiopentone 500 mg followed by suxamethonium 50 mg. The larynx was sprayed with 4 per cent lignocaine solution, and a cuffed endotracheal tube was passed. The lungs were inflated with nitrous oxide-oxygen mixture and pethidine 20 mg was given. He did not start to breathe, and at the end of the operation, about 45 minutes later, there was no response to carbon dioxide, nor to an intravenous injection of 2 ml nikethamide. He was returned to the ward, and artificial respiration was continued with nitrous oxide and oxygen; the apnoea was thought to be caused by suxamethonium, and arrangements were made for a transfusion of fresh blood. About two hours after the induction of anaesthesia spontaneous respiration started, regular but slow, and too shallow to maintain adequate oxygenation without assistance. Shortly afterwards a transfusion of one pint (592 ml) of fresh blood was set up, and it was then noticed that the muscles of the upper arms were

slightly wasted; this raised thoughts of muscular dystrophy, and it was decided to obtain a neurological opinion at a later date. A little later it was remarked that the type of respiration was now much more consistent with depression of the respiratory centre, and particularly resembled pethidine respiration. An intravenous injection of nalorphine 5 mg was given, with dramatic effect, and within five minutes and 3½ hours after induction of anaesthesia the patient was able to breathe adequately on his own. During this time the pulse and blood pressure had been within normal limits; serum potassium was 17 mg per cent (4.4 m. equiv/l) and serum pseudocholinesterase was 24.6 units (the normal range by the method of estimation being 13 to 31 units). He gradually regained consciousness, but by midnight, six hours later, he had developed pulmonary oedema. The chest was full of moist sounds, and the pulse was irregular and weak, rate about 90; the systolic blood pressure was 100 mm Hg. He was put on nasal oxygen, and was given 1 ml of 40 per cent alcohol by Collison's inhaler, repeated hourly. His breathing was much improved by morning, and he made an uninterrupted recovery over the next few days. It was noticed that his speech was at times a little difficult to understand and that some of his reactions were excessively emotional; this caused anxiety about his mental state, but it was ascertained from relatives that he had been so for some years. This helped to confirm the suspicion that he was suffering from myotonic dystrophy, and he was then referred to Dr. E. C. O. Jewesbury, who reported: "This is an interesting case of dystrophia myotonica. He is prematurely bald, has cataracts, loss of sternomastoids, weakness of limbs, slight wasting, myopathic speech, expression and gait, gonadal atrophy, and absent tendon reflexes, but no obvious myotonia. His father, also, was prematurely bald." X-ray screening showed normal diaphragmatic action. He has been followed up during the past twelve months, and has returned to work, and continues to lead a normal life; the ophthalmic result was excellent. When last seen he was engaged in painting the outside of his house, and his disability did not deter him from climbing ladders.

FIG. 1
A recent photograph, showing frontal baldness and myopathic facies.

INVESTIGATION

The patient was recently persuaded to receive test injections of thiopentone and pethidine while spirometry tracings were being taken, and these, together with a normal response (T.D.B.), are shown in figure 2.

The normal response to 50 mg of thiopentone shows an increase in the depth of respiration lasting about one minute; there was drowsiness for a short time but no loss of consciousness. There was no significant response to 10 mg of pethidine.

The patient responded to the same dose of thiopentone by two or three deep breaths followed by profound respiratory depression amounting to apnoea lasting for about one minute. Spontaneous breathing started at the moment that bemegride (Megimide) was injected, and this drug appears to have had no effect; again there was drowsiness only. After 10 mg of pethidine respiration slowed from 15 to 10 breaths per minute, returning to the previous rate after 8 minutes. It was not considered reasonable in a conscious patient to try the effect of suxamethonium great though the temptation; however, no abnormal reaction was noticed at the time of the operation, although it is interesting to note the reported aggravation of the myotonia by acetylcholine and neostigmine.

DISCUSSION

Only three cases of abnormal response to thiopentone in dystrophia myotonica have previously been reported (Dundee, 1952). In these cases the duration of narcosis appeared to be normal, and carbon dioxide failed to stimulate respiration; there was a very transient stimulation by nikethamide, which "suggests that the overaction of thiopentone is peripheral rather than central in origin and is probably an action

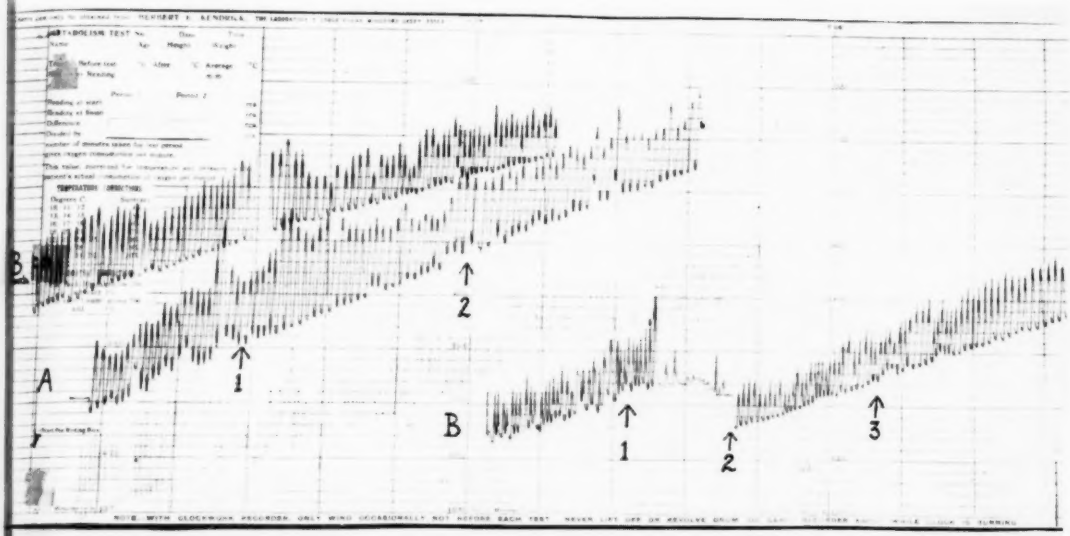

FIG. 2

Spirometry tracing, showing response to test injections of thiopentone and pethidine.

A. Normal volunteer. Weight 11 st 4 lb (71.7 kg).
1. Thiopentone 50 mg. 2. Pethidine 10 mg.

B. The patient. Weight 10 st 5 lb (66 kg).
1. Thiopentone 50 mg. 2. Bemegride 25 mg. 3. Pethidine 10 mg.

(The faint tracing is of the patient's respiration during acclimatization, and prior to the venepuncture.)

on abnormally sensitive muscles" (Dundee, 1956).

In the patient described above it is clear that at the time of operation there was, in addition to the thiopentone effect, central respiratory depression from papaveretum and pethidine; hence it was not possible at that time to relate the duration of narcosis, and the apnoea, directly to the dose of thiopentone. However, the subsequent investigation clearly demonstrated the abnormal effect of thiopentone, and the spirometry tracing could reasonably be interpreted as an initial central stimulation of respiration abruptly obscured by muscular paralysis as the drug reached the periphery. There was also, compared with the control, an increased response to pethidine, which in view of events at the time of operation appears to be of significance. It is doubtful whether this can be attributed solely to the relatively small difference in weight between the patient and the control. It is interesting to note this pethidine effect, which would seem to be central, in contradistinction to that of thiopentone.

It is attractive to attempt to relate the muscular effect of thiopentone to the abnormal creatine metabolism that occurs in dystrophia myotonica. Dundee (1956) discusses the tissue enzymes concerned in the metabolism of thiopentone, and refers to a cell-free homogenate of rat liver which is able to detoxicate the drug. "For maximum activity of this preparation cytochrome c, adenosine triphosphate, nicotinamide and a substrate are necessary." However, there is still considerable doubt about the mechanisms involved, for he later states "whether or not the energy for metabolic transformation of thiopentone is derived from Krebs cycle oxidations or from high-energy phosphate bond compounds result-

ing from these oxidations is not established. A complete inhibition of phosphocreatine synthesis, by 2.4 dinetrophenal, depresses thiopentone metabolism by only 30 per cent, suggesting that a source of energy other than phosphocreatine stores is available for the breakdown of the drug." Thus there remains ample scope for speculation and, perhaps more profitable, for research.

CLINICAL IMPLICATIONS

Although this is a rare disease, it is stated that at least 50 per cent of patients develop cataracts, and it seems likely that anaesthetists may be faced more often with the problem of the patient suffering from dystrophia myotonica if the present trend towards general anaesthesia for ophthalmic surgery continues; and the disability may not be obvious. Thus in the younger patient with cataracts both diabetes mellitus and dystrophia myotonica must be born in mind, and it should also be remembered that these conditions can co-exist. Local anaesthesia is the method of choice, but if for any reason it is desired to use thiopentone it should be given very dilute, and a 1 per cent solution is suggested for controllability, although it has to be considered whether apnoea might occur without loss of consciousness; Dundee (1956) recommends that the dose should not exceeed 100 mg. If a large dose is given by mistake the patient may regain consciousness before breathing becomes adequate, and because of this, and for physiological reasons, artificial respiration must be maintained with nitrous oxide and oxygen, not with oxygen alone. It would also appear that these patients need smaller doses than normal of pethidine and other respiratory depressants. Another condition in which the presence of this disease may be considered is adenoma of the thyroid, although the association must be extremely rare. It is not known whether the same susceptibility exists to thiopentone when the disease is latent, and there is probably no means of knowing until after the event; the patient described above has no children, so it was not possible to investigate this aspect of the problem.

ACKNOWLEDGMENTS

We are indebted to Mr. J. Gibson Moore and to Dr. E. C. O. Jewesbury; to our colleagues Dr. P. W. Spencer Gray and Dr. S. C. Van der Merwe; to Mr. R. A. Lee, Senior Laboratory Technician; and to Messrs. E. & S. Livingstone, Ltd., for permission to quote from Dr. Dundee's book.

REFERENCES

Dundee, J. W. (1952). *Curr. Res. Anesth.*, **31**, 257.
—— (1956). *Thiopentone and other thiobarbiturates*, pp. 53, 55, 182. Edinburgh: Livingstone.
Wright, S. (1952). *Applied Physiology*, London, O.U.P.

Brit. J. Anaesth. (1957), **29**, 39

A MODIFICATION TO THE TRICHLOROETHYLENE VAPORIZER ON THE "BOYLE" APPARATUS

BY

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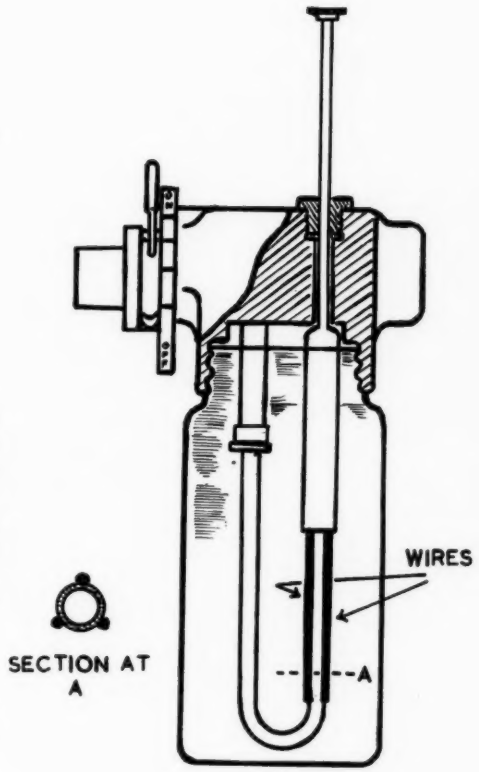
AN investigation of the vapour concentrations delivered by the trichloroethylene vaporizer of a Boyle's apparatus revealed the need to keep the cowl of the plunger at all times concentric with the U-tube outlet (Mapleson, 1957). This can be ensured by soldering three vertical copper wires equally spaced around the U-tube. The cowl can still be pulled up and down easily whilst concentricity is maintained.



REFERENCE

Mapleson, W. W. (1957). Trichloroethylene Concentration from a "Boyle" Type Anaesthetic Apparatus. *Brit. J. Anaesth.*, **29**, 3.

Brit. J. Anaesth. (1957), **29**, 40

A SEMI-AUTOMATIC BLOOD PRESSURE RECORDER

BY

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IN the recent past a number of blood pressure recorders for clinical use, and especially during anaesthesia, have been described (Molyneux and Pask, 1953; Simpson, 1956). It seemed, however, that these recorders had several disadvantages and that there was a place for an instrument that was cheap, simple and not a possible source of an explosion when used in the vicinity of explosive anaesthetic agents, provided that this could be done without too great a sacrifice of efficiency.

The instrument (fig. 1) described below enables records of systolic blood pressure to be obtained at frequent intervals though it is in fact sphygmotonographic in principle. It is also probably simple and cheap enough to be used alone as an aid to the taking of routine blood pressures during anaesthesia. By means of an inflating device a single blood pressure cuff with a brachial stethoscope beneath is inflated to a predetermined but variable level. Oxygen from the anaesthetic machine is used for this purpose. The oxygen escapes through two holes, one of fixed size, the other variable so as to achieve a more or less linear fall of pressure. On hearing the Korotkov sounds the operator reinflates the cuff and the cycle is repeated. The inflator is designed to be operated by the foot, thus freeing the hands for the giving of the anaesthetic or for performing such other manoeuvres as one wishes, for example, signalling events upon the recording drum.

DESCRIPTION OF THE INSTRUMENT

The cuff inflator is contained in a brass box measuring $16 \times 8 \times 8$ cm. The lid is detachable and carries the operating pedal which works in a plain bearing lubricated, as are all moving parts, with a noninflammable grease. A rubber washer ensures an airtight fit between the lid and the box, as do fibre washers beneath the heads of the securing screws. It works as follows:

Depression of the foot pedal opens the oxygen tap. The tap is a modified M.I.E. injector sucker

FIG. 1

tap with a rubber instead of a Neoprene valve seat, and with a lighter spring. In addition to opening the oxygen tap, depression of the operating plunger allows the control rod to move forward into the slot A (fig. 2), thus holding the tap open. The control rod is attached to a metal bellows which is spring loaded. When the pressure inside the box and cuff rises the bellows is compressed and the control rod moves back, allowing the tap to close. This cut-off pressure is determined by the extent to which the spring is initially compressed by the screw seen on the right. The size of the bellows and its spring is not critical, a bellows from a bomb sight computer was used in the inflator shown.

The oxygen now escapes through the two holes. The variable hole can be seen on the front of the instrument. A gramophone needle soldered to a small metal bellows (also from a bomb sight computer) moves in and out of the hole as the pressure inside rises and falls, the inside of the small bellows being connected to the inside of the inflator. This ensures that the rate of fall of pressure is more or less constant. In addition, the fixed hole is provided with a tap so that the rate of fall can be adjusted. The inflator is connected to the sphygmomanometer cuff, to the recorder, and it is useful also to have in the circuit a mercury column so that the blood pressure can be read directly and the rate of fall checked.

The recorder consists of an ink writer on a movable arm, the arm being connected to a metal bellows, thus tracing the pressure cycle in the cuff. As the pressure rises each time the pedal is depressed on hearing the systolic sound, a tracing of the type shown in figure 3 results, the systolic pressure being at the lowest point of the pen travel. If desired, a record of both systolic and diastolic pressures, with or without a fall to zero of the pressure in the cuff, can be obtained.

DISCUSSION

Approximately 4 seconds is required to inflate the cuff to 200 mm of mercury, less for lower pressures. Any greater rate tends to operate the cut-off before the desired pressure is reached in the cuff due to inertia in the tubing.

The rate of fall is determined by the ease and certainty with which one can hear the Korotkov sounds and also by the pulse rate, a slower pulse rate giving a greater error for each missed sound. I find that the maximum rate of fall that can be used is about 10 mm per second.

In practice the control is set to blow off at some

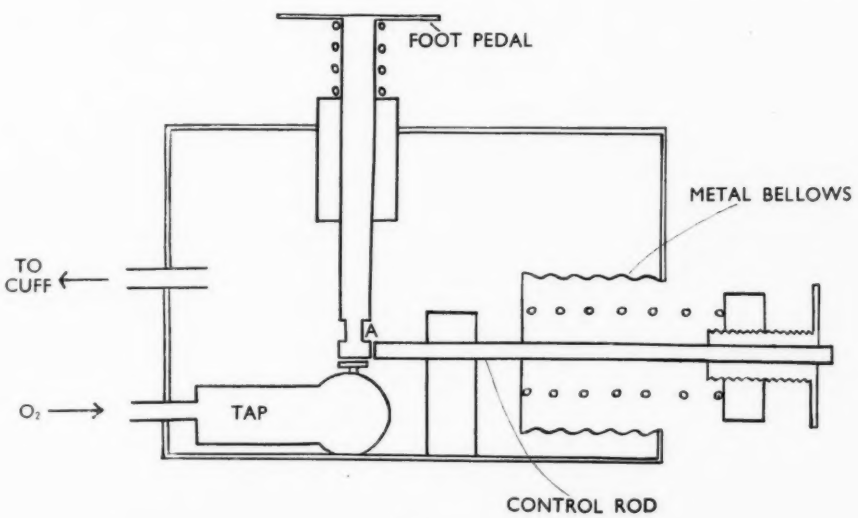

FIG. 2

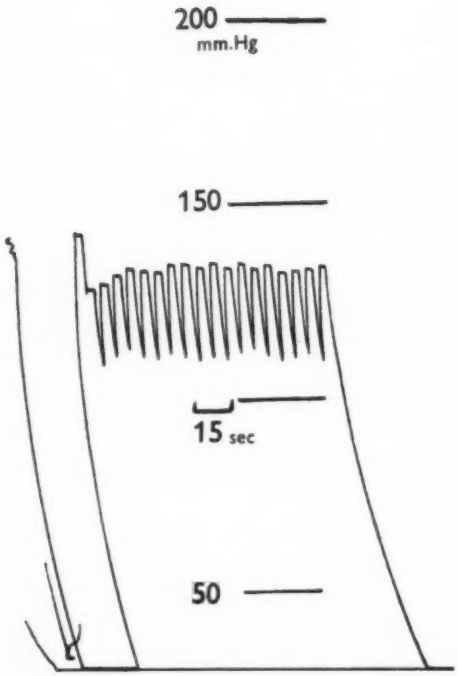

FIG. 3

level above the systolic blood pressure in order to give time to hear the sounds and also because friction in the control rod bearing prevents it from re-engaging in the slot immediately after it has blown off. The amount of fall required for this varies with the cut-off pressure. About 55 mm fall is required from 200 mm of mercury, about 30 mm from 140 mm of mercury. The actual level of the systolic blood pressure, therefore, also determines the number of readings that can be taken in a given time. As the blood pressure rises or falls the spring tension can be increased or decreased so that as little time as possible is wasted, having regard, of course, to the limitations mentioned above. Under good conditions it is possible to record the systolic blood pressure every 5 seconds.

The linear fall device is necessary so that the fall of pressure in the lower ranges will not be unduly slow—or unduly quick at high pressures, as would occur with a fixed orifice—and enables readings to be taken more frequently.

Events can be signalled on the drum with an ordinary sphygmomanometer bellows, which is given a smart squeeze while the pressure is falling. A notch is thus produced in the record.

If it is desired to record both the systolic and diastolic pressures then the systolic pressure can be signalled with the bellows and the diastolic by the lowest point of the trace as the pressure rises once more. Alternatively both systolic and diastolic pressure can be signalled with the bellows and the pressure allowed to fall to zero between each reading.

It is more satisfactory if one's whole time can be devoted to the recording of the blood pressure, but with a little practice recording can be done by the person giving the anaesthetic and readings taken during the course of intubation, for example.

SUMMARY

A blood pressure recorder of sphygmotonographic type is described.

It requires an operator but is simple, cheap and nonelectrical.

Under the best conditions the systolic blood pressure can be recorded every 5 seconds.

Both systolic and diastolic blood pressures can be recorded with or without a fall to zero pressure in the arm cuff.

ACKNOWLEDGMENTS

The apparatus was described at a meeting of the North of England Society of Anaesthetists on March 16, 1956.

I should like to acknowledge the encouragement of Dr. R. P. Harbord.

The prototype was made with minimal workshop facilities but the model illustrated was made for me by Newcastle Scientific Apparatus, 61 Tavistock Road, Newcastle upon Tyne, the cost being met by a grant from the Department of Anaesthesia of the University of Leeds.

REFERENCES

Molyneux, L., and Pask, E. A. (1953). *J. Physiol.*, **121**, 13.

Simpson, D. C. (1956). *Anaesthesia*, **11**, 89.

ON CHLOROFORM AND OTHER ANÆSTHETICS

THEIR ACTION AND ADMINISTRATION

BY

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Licentiate of the Royal College of Physicians

(*Continued from Vol. XXVIII, page* 531)

The foregoing cases comprise all the instances I have seen recorded in which death appears to have been occasioned by the administration of chloroform, and not by other causes in operation about the same time. A few additional cases have indeed been referred to by different authors where death was probably caused by chloroform, but as I do not find that the details have been published, I cannot make them available in an inquiry respecting the cause and prevention of these accidents.

In June 1852, Dr. Simpson alluded in the following terms to an accident from chloroform which had occurred near Glasgow: —" In this instance, chloroform was given by the practitioner for tooth extraction; but, I am sorry to add, none of the parties present were at the time in a condition to give any satisfactory evidence."*

A person, named Breton, a dealer in porcelain, died in Paris, in the early part of 1853, immediately after a few inspirations of chloroform, which was administered with the intention of removing a tumour of the cheek. An action was brought against Dr. Triquet and M. Masson for causing death by imprudence in this case; and at the trial which ensued, various interesting opinions were given, and the accused practitioners were ultimately exonerated.* I have not, however, met with any record of the symptoms which occurred in the case.

In relating the case of death from chloroform, which occurred in his practice, to the Medical and Chirurgical Society of Edinburgh, Dr. Roberts referred to another death from chloroform in tooth-drawing which took place in the neighbourhood from which his own patient came, just previously to October 1855; but I have not met with any account of the case alluded to. Dr. Mackenzie of Kelso also alluded in the same Society, in the following year, to a death from chloroform which had occurred at Coldstream, and I do not know whether this was the case to which Dr. Roberts had alluded, or a fresh one.

One of the surgeons at the hospital at St. Louis, who was lately visiting the medical institutions of London, informed me that there had been three deaths from chloroform at his hospital out of between six and seven hundred operations in which

* Med. Times and Gaz., 1852, vol. i, p. 627.

*Gaz. Médicale, 1853, p. 304.

it had been administered. I did not learn the particulars of those fatal cases.

There have been several cases in which persons have been found dead after inhaling chloroform when no one else was present, either for toothache or some other affection, but I have not included such cases in the above list, as they throw no light on the way in which death is occasioned. The simple way to avoid such accidents as those just alluded to, is for persons to abstain from inhaling chloroform, when no one is by to watch its effects.

ALLEGED FATAL CASES OF INHALATION OF CHLOROFORM

Several deaths have been attributed to chloroform which were due to other causes, or where the cause of death is a subject of great doubt. A gentleman, named Walter Badger, twenty-two years of age, the son of one of the coroners for the county of York, died instantly at Mr. Robinson's, the dentist's, in Gower Street, on June 30th, 1848, whilst commencing to inhale chloroform with the intention of having some teeth extracted. The inhaler employed consisted of a face-piece to enclose the mouth and nostrils, and containing a sponge on which the chloroform (ʒ iss) was placed. This, according to the evidence of Mr. Robinson and his female servant, who was present in the room, was held not nearer than an inch and a half from the face for less than a minute, and the patient made the remark that the chloroform was not strong enough; Mr. Robinson requested him, as he had done before, to have the operation performed without chloroform, but he again declined; and Mr. Robinson then took away the face-piece and asked his servant to reach the bottle intending to put more chloroform on the sponge, to replace that which he believed had been lost by evaporation. Just after removing the face-piece, and before any fresh chloroform was poured out, the head and hand of the patient dropped, and he did not show any further sign of life.

I found, on making trial of the kind of inhaler which Mr. Robinson employed, that it is impossible to inhale enough of the vapour to produce any appreciable effect, unless it is applied so as to touch the face. At the distance of an inch no effect is produced, even in five or ten minutes; and therefore I expressed my opinion, soon after this accident, that it was not caused by the chloroform, which properly speaking the patient did not inhale.

A consideration of the symptoms in this case confirms the view that the death was not caused by chloroform. In six of the fatal cases related above, death took place instantaneously, without insensibility or any of the usual effects of chloroform having been produced; but the mode of dying was not the same as in Mr Robinson's patient. In Case 4, that of Madlle. Stock, the patient said "I choke", and tried to push away the handkerchief; then there was embarrassed breathing and foaming at the mouth. In Case 11, that of Madame Labrune, the fatal attack followed immediately on a full inspiration of chloroform, and there was an immediate alteration of the features, and a convulsive rolling of the eyes, amongst other symptoms. In Case 14, the young lady stretched herself out, and frothed at the mouth, at the moment of the fatal attack,

and the face became livid. In Case 26, that of Madame W., who died at Ulm, the voice, when answering the question about singing in her ears, was trembling and thick; she stretched out her limbs, and the face became bluish. In Case 45, that of the wife of a medical man, and in 46, that of Dr. Roberts's patient in Edinburgh, there was a convulsive start at the moment of the sudden death. It thus appears, that when the heart is suddenly paralysed by an overdose of chloroform, before the patient is rendered insensible, there are usually some symptoms as if of a violent shock or injury. After complete insensibility is induced, the heart may be suddenly paralysed by chloroform, as is shown by numerous cases, without this spasmodic action; and it would perhaps be premature to deny that a patient might die thus quietly without being first made insensible; and the nature of the death in this particular case must be chiefly decided by the physical fact that the patient could not have inhaled enough chloroform to produce an appreciable effect of any kind, much less to cause sudden death.

At the inspection of the body, the liver was found so much enlarged that it weighed eight pounds, and it encroached very much on the chest. The walls of the left ventricle of the heart were found thinner than natural, and the muscular tissue was interspersed with fatty degeneration. There was blood in the right auricle and in both ventricles. In the ventricles it was partly coagulated. The brain presented nothing abnormal.*

It is probable that the immediate cause of death in this instance was fear. The patient had been told in the country that it would be unsafe for him to take chloroform, and yet he could not summon resolution to undergo the operation without it. Mr. Robinson unfortunately allowed his patient to remain seated in the operating chair; and it was only when Dr. Waters had been sent for and arrived from a neighbouring street that he was laid on the floor.

I was present on one occasion with Mr. Peter Marshall at the examination of the body of a woman who died suddenly of fright in consequence of a fire in the next house to that in which she lived, and it is worthy of remark that we found exactly the same diseased conditions as those which were found in Mr. Robinson's patient; viz., great enlargement of the liver, displacing the viscera of the chest, and fatty degeneration of the heart.

A young man, aged twenty-four, died suddenly of syncope, on June 25th, 1848, at the Hospital Beaujon, at Paris, whilst M. Robert was performing amputation at the hip joint, the thigh bone having been broken into splinters by a bullet during the conflict in the streets of Paris. The patient was in a state of great depression, both physical and moral, before the operation; and it is most likely that he sank under the combined effects of the injury and the operation.

Another patient had the neck of the humerous broken by a ball in the same conflict; he was much reduced by hæmorrhage and gangrene of the wound; M. Malgaigne performed disarticulation at the shoulder joint; a fresh inhalation took place to enable him to search for the ball, and the patient sank and died during the last incisions. This patient also most

* Lancet, 1848, vol. ii, p. 47.

probably died from the effects of the operation added to those of the previous injury and loss of blood.

A woman died in Paris, 1848, after removal of the breast. The operation was finished, and the chloroform had been left off some time, and the patient had become conscious, when on raising her into a sitting posture, in order to apply a bandage, she suddenly expired. Although the chloroform was blamed in this instance, death evidently took place by the ordinary kind of syncope, which arises from the heart not being supplied with blood, and which may be called anæmic syncope, in contradistinction to cardiac syncope, which begins at the heart itself, when properly supplied, or even when distended with blood.

A child, aged twelve years, died in the hospital at Madrid in 1849, during amputation of the leg after violent tetanic rigidity.* Death was attributed to the chloroform which had been inhaled, but no further particulars are given, and it is not stated whether or not there was any unusual hæmorrhage, or other cause, which would explain the fatal event.

Dr. Aschendorf has attributed the death of a child a year old to chloroform.† The child had a nævus on the face and neck, which extended from the zygoma to the os hyoides, and from the external auditory meatus to the maxillary fossa. No one had been willing to undertake its removal. Dr. Aschendorf operated on the nævus at three different times, by means of seton threads. These operations were performed under the influence of chloroform. The tumour was reduced one-third part in size by these means, and eleven weeks afterwards Dr. Aschendorf determined to extirpate it. The chloroform was administered as on the former occasions, by placing six drops on some tow in a cup. In about ten minutes, as the child cried a little, three drops more of chloroform were used for inhalation, and in about eight minutes more the operation was concluded. "On raising the child it laid its head on one side, convulsive twitches of the face were observed, with distortion of the eyeballs and dilatation of the pupils. For one moment the arms were stretched out stiff, then again they were relaxed, and fell as supple as the rest of the body. Death quickly followed—only one pulsation of the heart and a single râle with the expiration being perceived.

There can be no doubt of this being a case of death from hæmorrhage, after the direct effects of the chloroform had subsided. Dr. Aschendorf says the quantity of blood lost was about two tablespoonfuls; but it would be necessarily removed by sponges during the operation, and there would be no means of estimating the quantity. The child was probably in a state of syncope during the latter part of the operation, as it would not remain insensible to the knife for eight minutes from a single application of chloroform.

* Bouisson, Méthode Anesthésique, p. 398.

† Casper's Wochenschrift, September 6, 1850; and London Med. Gaz., vol. xlvii, p. 261.

(*To be continued*)

CORRESPONDENCE

POTASSIUM DEPLETION AND THE CENTRAL ACTION OF CURARE

Sir,—Dr. Patrick A. Foster is to be congratulated for writing so freely about unsuccessful cases, and his paper ("Potassium Depletion and the Central Action of Curare," *Brit. J. Anaesth.* (1956), **28**, 488) must have been read with great interest by many. I wonder however, whether his cases really illustrate the thesis which he maintains: after all, there are other causes of both central and peripheral neuromuscular depression.

For example, Dr. Foster's Case No. 7 was obviously in a poor state. She had been vomiting for 24 hours, no doubt her ability to breathe was limited by abdominal distension, she had apparently received inadequate intravenous therapy, and was given what may well have been an excessive dose of morphine for one so ill. Not surprisingly, she had "prolonged post-operative sleep" and "had no remembrance of induction or intubation." The comment states, "This is thought to provide an unequivocal instance of a central action of dTc", but, to me, it conveys no such impression. Does one need to postulate such an hypothesis to account for struggling or apparent unconsciousness on administering 10 mg of d-tubocurarine to such a patient?

By the way, is it common practice to administer neostigmine in such large doses? In the three cases in which the total dose is mentioned it is given as 15 mg, 15 mg, and 20 mg. With the doses of d-tubocurarine used, I should have expected 2.5 mg to produce complete reversal of the relaxant and I should have assumed that any subsequent failure to breathe was due to some other cause. Although I often use d-tubocurarine in comparable doses, my custom is to give an initial dose of neostigmine, 1 mg, followed, if necessary, by not more than two further doses of 0.5 mg. The total dose of 2 mg is only exceeded with the greatest reluctance. Surely doses of the order mentioned may have contributed substantially to the apnoea and must have played Old Harry with the heart and intestinal tract, to say nothing of every other organ in the body.

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Sir,—As with any new and unanticipated event, the records thereof are not as full of relevant data, nor as convincing, as could be wished. The article was an attempt to define a clinical picture from fragments collected in a number of cases of apparently similar nature. Whether the thesis is correct is at present a matter of opinion, awaiting further evidence. But there are not many known causes of persistent neuromuscular block by antidepolarizing agents where efficient circulation and ventilation have been maintained, where nitrous oxide without hypoxia has been the only narcotic, and where no postmortem lesion could be found.

I regret that case report No. 7, receiving Dr. Armstrong-Davison's attention, may have conveyed a wrong impression. Dr. Armstrong-Davison follows the pre-operative and post-operative course of his patients perhaps more thoroughly than many other anaesthetists, and his criticism is thus valued, but not here apposite. This lady was in good condition, and no extensive pre-operative preparation was considered necessary. She was not grossly distended nor dehydrated; in fact, she was the type of case that would not normally cause the anaesthetist anxiety, and who would have been unremarkable had the unorthodox technique not been used.

As an observer, not the administrator, of the anaesthetic, I was able to remark, I hope accurately, on the disappearance of eye signs usually thought to be absent only in relatively deep planes of unconsciousness. She came to the operating theatre obviously fully in touch with her surroundings, with subsequent recall of events com-

plete to the time of injecting the curare, before the use of nitrous oxide.

No, I believe that this was definite unconsciousness, not apparent unconsciousness.

The type of cases reported, being surgical emergencies, are frequently handled by non-consultant staff. My critic is aware of the frailties of human nature, and of the likely reaction when the antidote one has been taught to trust is ineffective. In such a nightmare situation, one does tend to flog the tired horse—and run up a startling blood level of neostigmine. This would seem a dangerous practice, although by some accounts not lethal (cf. recent correspondence in the *Brit. med. J.*, 1956, **2**, 1114, where there is an account of an old woman surviving 40 mg!).

However, several times was mention made in the article of the possible baleful influence of neostigmine as a factor in the fatal outcome: yet it should be emphasized that signs of an abnormal response to curare preceded the use of neostigmine.

What the correct dose of neostigmine should be seems to be a hardy perennial subject of argument. Suffice it to say that a routine dose of 5 mg for reversal of curarization is safely given in Liverpool (and Cape Town!), but only after an adequate muscarinic blocking dose of atropine has taken effect. Perhaps Old Nick attended the reported cases, but it is remarkable how consistently absent is Old Harry when sufficient atropine suppresses his fulminations.

What is at present most difficult is to unravel the interplay of central and peripheral effects of curare against the distracting backlighting of neostigmine action. Both curare and neostigmine are drugs with undoubted ability to produce profound central interference in appropriate circumstances. Yet the transient improvement produced by neostigmine in these cases, declining with subsequent doses, is strangely reminiscent of the action of this drug on muscle in which cholinesterase has been destroyed by DFP (Riker and Wiscoe, 1946). Significantly, DFP is an anticholinesterase capable of destroying the enzyme it inhibits, but unlike other anticholinesterases, may synergize with curare (Barstad, 1956). It would seem that our attention should focus on muscle and brain cholinesterase systems rather than on blood pseudocholinesterase systems which at present largely occupy it.

It is my hope that the account of our misfortunes, apart from making general anaesthesia safer, will point the way to the solution of a problem of fundamental importance to our science.

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REFERENCES

Barstad, J. A. B. (1956). *Arch. int. pharmacodyn.*, **107**, 275.

Riker, W. F., and Wiscoe, W. C. (1946). *J. Pharmacol.*, **88**, 58.

CARDIORESPIRATORY ARREST FOLLOWING LOCAL ANAESTHESIA

Sir,—I read with interest a report of a case of cardiorespiratory arrest following local anaesthesia as described by Dr. R. R. Gilfillan (*Brit. J. Anaesth.* (1956), **28**, 524), where 2 ml of 1 per cent amethocaine with adrenaline was run into each main bronchus. The speed of absorption from the lungs has been shown to equal intravenous injection (Shumacker, 1941). Though the addition of adrenaline to solutions for topical application has been advocated (Carabelli, 1952), animal experiments (Rubin, 1951; Keil and Vieten, 1952) demonstrated that for adrenaline intratracheally to be effective in lowering toxicity, it must be administered prior to the local anaesthetic. If both drugs are administered together there is an increase in toxicity. There would thus appear to be little justification for the intratracheal administration of adrenaline with a local anaesthetic. I would also make a plea that 0.25 per cent amethocaine would permit a wider dispersion of what is still an effective concentration of anaesthetic (Clark et al., 1954).

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REFERENCES

Carabelli, A. A. (1952). *Anesthesiology*, **31**, 169.

Clark, R. E., Orkin, L. P., and Rovenstine, E. A. (1954). *Anesthesiology*, **15**, 161.

Keil, W., and Vieten, H. (1952). *Fortschr. Geb. Röntgenstrahlen.*, **76**, 796.

Shumacker, H. B. (1941). *Surgery*, **10**, 119.

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